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ARCHIVES OF SURGERY

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# THE ETIOLOGY OF POSTOPERATIVE PEPTIC ULCERS

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One of the most serious and distressing complications following surgical treatment for benign gastroduodenal ulcerations is the postoperative peptic ulcer. Jejunal ulcers following gastro-enterostomy have been reported frequently in the literature. It appears that no method of surgical procedure offers an absolute assurance against this much dreaded complication. In 1921, Denk [1] reported six cases of definite peptic ulcers and eight doubtful cases following resection of the stomach. In 1925, Birgfeld [2] reported fifty-three cases of jejunal ulcerations following the Billroth II method of resection of the stomach. In a summary of 13,000 resections of the stomach Starlinger [3] reported 0.9 per cent recurrent ulcerations after the Billroth I method of resection, and 0.6 per cent jejunal ulcerations after the Billroth II method of resection.

There is a great deal of discussion in the literature concerning the etiology of this complication and the surgical methods most effective in its prevention. The main object of our work has been to study the principles involved in the mechanical and chemical factors concerned in the etiology of peptic ulcers.

In the last decade much has been written in regard to gastritis, duodenitis and jejunitis, which are found concomitant with peptic ulcerations. Some of the investigators are of the opinion that these inflammations and ulcerations of the gastro-intestinal mucosa are of infectious origin. Saunders [4] has recently isolated streptococci from ulcers obtained

From the Physiology Department of the University of Oregon Medical School.

1. Denk, W.: Ueber Aetiologie und Prophylaxe des postoperativen Jejunalgeschwüres, Wien. klin. Wchnschr. **34**:2 (Jan. 6) 1921; Studien über die Aetiologie und Prophylaxe des postoperativen Jejunalgeschwüres, Arch. f. klin. Chir. **116**:1 (July 21) 1921.

2. Birgfeld, E.: Ueber das Ulcus pepticum jejuni nach Magenresektion, Arch. f. klin. Chir. **137**:568, 1925.

3. Starlinger, F.: Das Rückfallsgeschwür nach Magenresektion wegen Ulcus ventriculi oder duodeni, Arch. f. klin. Chir. **162**:564, 1930.

4. Saunders, E. W.: Serologic and Etiologic Specificity of Alpha Streptococcus of Gastric Ulcer: Bacteriologic Study, Arch. Int. Med. **45**:347 (March) 1930.

from human material which he claims to be specific after cultural tests and agglutinations. The theory of focal infection of Rosenow has caused many "foci of infection" to be removed with the hope of curing the peptic ulcerations. Steinberg [5] pointed out that the focal infection, particularly in relation to the etiology of peptic ulcer, deserves a more critical interpretation. He has called particular attention to the vulnerability of the mucosa of the stomach in the presence of acid pepsin when either the local or the general resistance of the animal is lowered. This condition frequently takes place when the animal is subjected to violent experimentation, particularly the intravenous injection of various sorts of substances. It is no wonder that an army of experimental workers has been successful in producing acute lesions of the gastroduodenal mucosa, utilizing different methods of experimentation.

It is common knowledge that there are exceedingly few primary ulcers of the jejunum; it is only when the stomach is directly anastomosed with the jejunum that typical ulcers occur. Since the acid pepsin possesses bactericidal properties one would hardly expect that the surgical procedure in gastro-enterostomy would influence the growth of bacteria and that this would be the primary cause of ulcer formation. Later in our experiments it will be seen that when the acid is neutralized by the bile and pancreatic juice, no ulcers occur. It is difficult to deny, however, in view of the bacteriologic studies, particularly of Saunders,[4] that the infection plays some part in the chronicity of the ulcer. It is possible that a peptic ulcer offers favorable conditions for growth of the particular organism isolated by this investigator.

Silk or linen is frequently found to protrude into the gastroenterostomy opening. Hilarowicz [6] expressed the belief that the secretions of the stomach may penetrate into the canal formed by the silk and produce an ulceration. That the injury caused by the silk suture may be responsible for some acute and perforated ulcerations was proved by one of our recent experiments in which two ulcerations about 4 by 5 mm. each occurred exactly where the silk penetrated the intestinal wall. However, many ulcers are found in which absorbable suture material is used, and numerous ulcers are also located remote from the line of anastomosis. We therefore hold the unabsorbable material responsible for only a very small number of postoperative peptic ulcerations.

5. Steinberg, M. E.: Stomach Mucosa in Ulcer and in Carcinoma, Arch. Surg. **14**:991 (May) 1927.

6. Hilarowicz, H.: Ein experimenteller Beitrag zur Frage der Bedeutung der Seidenfäden für das Entstehen des postoperativen Jejunalgeschwüres, Zentralbl. f. Chir. **10**:379, 1924.

Klose and Rosenbaum-Canné [7] studied the question of intestinal clamps in relation to the formation of postoperative peptic ulcers and found that they are of no importance. Ulcers are frequently found in cases in which no clamps have been used; some ulcers are located at the insertion of the mesentery and in the distal loop remote from the anastomosis, where no circulatory disturbance from the clamps could have taken place. Recently we observed a patient who was operated on for two jejunal ulcerations following gastro-enterostomy; one was located opposite the gastro-enterostomy opening at the insertion of the mesentery, and the other was found about 5 cm. from the distal end of the gastro-enterostomy opening on the anterior wall of the jejunum penetrating into the colon. The surgeon who performed the gastro-enterostomy used no clamps.

Montgomery,[8] in sixty-three experimental gastro-enterostomies, found four ulcers. All of these took place in the line of the anastomosis, where a hematoma was purposely produced. Since a great many ulcers are found remote from the gastro-enterostomy suture line, and some several years after the operation, the hematoma may be considered as only a casual factor in this complication.

### CHEMICAL AND MECHANICAL FACTORS

From the time of Hunter [9] there have been numerous experiments to prove that the mucosa of the stomach is more resistant to the destructive power of the acid gastric juice than the other tissues. In order to study the effect of gastric juice on the jejunal mucosa, Bickel [10] excluded the duodenal secretions of the liver and pancreas by implanting their ducts into the abdominal wall. Utilizing this method, he obtained postoperative peptic ulcers. Exalto [11] reproduced in animals the same operative procedures used in man to cure gastroduodenal ulcers. He severed the stomach immediatly above the pylorus and formed a posterior gastro-enterostomy either with the duodenum or the jejunum in seven cases, but was not able to produce any ulcers. On the other hand, in three of four cases he was able to produce ulcers when, in addition to the foregoing measures, he also formed a Roux anastomosis. In the last

7. Klose, H., and Rosenbaum-Canne, P.: Vergleichende experimentelle Untersuchungen über die Magennähte, Arch. f. klin. Chir. **124**:15, 1923.

8. Montgomery, A. H.: Gastrojejunal Ulcer: An Experimental Study, Arch. Surg. **6**:136 (Jan.) 1923.

9. Hunter, J.: On the Digestion of the Stomach After Death, Phil. Tr., London **62**:447, 1772.

10. Bickel, A.: Beobachtungen an Hunden mit extirpiertem Duodenum, Berl. klin. Wnchschr. **46**:1201, 1909.

11. Exalto, J.: Ulcus jejuni nach Gastroenterostomie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **23**:13, 1911.

three cases he anastomosed the distal part of the duodenum to the large bowel, thus excluding the alkaline duodenal contents from the upper part of the jejunum, and obtained ulcers in all the cases. With the exception of the last dog, all the others received hydrochloric acid by mouth.

According to the observations of Stahnke,[12] jejunal ulcers were nearly always found in the distal loop of the jejunum following gastroenterostomy and lateral anastomosis. In addition to the ulcers, there was, in every case, a swollen, red mucosa covered by mucus. This condition of the mucosa was always observed sharply at the beginning of the distal portion directly within the anastomosis and reached in the distal portion exactly as far as the lateral anastomosis, or to where the doudenal contents began again to bathe the mucosa. The same condition was noted by Hertel[13] in a dog with a Billroth II anastomosis. Finsterer,[14] Schnitzler,[15] Lorenz and Schur[16] and others have emphasized the importance of using surgical procedures that reduce the acidity of the gastric contents and therefore remove one of the causes of jejunal ulcerations. These clinicians have noted the striking change in the chemistry of the contents of the stomach after resection of the stomach. Lorenz and Schur[16] have reviewed a series of their cases following partial gastrectomy. They have noted that the size of the antrum removed was directly proportional to the reduction of the acidity. They laid particular emphasis on the fact that the removal of the antrum does away with the part of the stomach that is indirectly responsible for the chemical phase of the gastric secretion. Steinberg, Brougher and Vidgoff[17] have definitely proved that the most important factors in the reduction of acidity after resection of the stomach are the rapid emptying of the stomach and the neutralization of the contents of the stomach by the influx of the alkaline juice from the duodenum. Since peptic ulcers have been reported following resection of the stomach, Finsterer[14] has advised removal of from three fourths to four fifths of the stomach in order to do away with part of the actual

12. Stahnke, E.: Zur Frage der Braun'schen Anastomose, Vereinigg. d. bayer. Chir., 1926; abstr., Zentralbl. f. Chir. **53**:2946 (Nov. 13) 1926.

13. Hertel, E.: Die Entstehungsursachen des postoperativen Jejunalgeschwüres, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **42**:57, 1930.

14. Finsterer, H.: Ueber die Bedeutung der Magenresektion beim Ulcus duodeni, Zentralbl. f. Chir. **52**:954, 1918.

15. Schnitzler, V.: Die Anwendung der ausgedehnten Magenresektion zur Behandlung des Magengeschwüres, Med. Klin. **17**:564 (May 8) 1921.

16. Lorenz, H., and Schur, H.: Unsere Efahrungen über den Wert der Antrumresektion beim Ulcus pepticum, Arch. f. klin. Chir. **119**:239, 1922.

17. Steinberg, M. E.; Brougher, J. C., and Vidgoff, I. J.: Changes in the Chemistry of the Contents of the Stomach Following Gastric Operations, Arch. Surg. **15**:749 (Nov.) 1927.

acid-secreting area of the stomach. These surgical procedures were always based on the theory that acid pepsin was the supreme factor in postoperative jejunal ulcerations.

The postoperative jejunal ulcers following the exclusion operation introduced by von Eiselsberg, in which the pylorus was not removed, were frequent. Von Haberer [18] found this complication in 20 per cent of his cases, and Clairmont [19] in 28 per cent. These facts were of extreme importance and interest, since they emphasized not only the danger of such an operation but also its importance as an etiologic factor in jejunal ulcerations. Schur and Plaschkes [20] believed that in the excluded part of the pylorus the contents of the stomach and duodenum are accumulated and stimulate an increased production of acidity in the fundus.

Aschoff [21] has emphasized the "Magen Strasse," which is the fixed lesser curvature of the stomach, as of etiologic importance in ulcer formations. The conformation of the pyloric motor part of the stomach, the isthmus, which is the physiologic narrow pass, and the duodenal cap, which is the bumper for the peristaltic waves of the muscular pylorus, have been advanced as the cause of ulcer. Some such mechanical factors and insults find a parallel in the gastro-intestinal anastomosis. The force of the flow of the contents of the stomach, however, is not under the same control in a gastro-enterostomy as through the pylorus; the contents passing through the gastrojejunal opening may be more passive. The wall of the intestine against the stomach receives the flow of the gastric contents. The observation of Denk,[1] that the seat of the ulcer is on the anterior wall of the distal loop, is in agreement with the theory of a mechanical insult.

Chiari [22] has demonstrated that postoperative ulcers in the majority of cases are found at the insertion of the mesentery and in this way are also analogous with the location of the ulcers of the stomach along the lesser curvature, where the gastrohepatic omentum is inserted. The same author expressed the belief that the fixation of this part of the intestine to the stomach and the adhesions about the anastomosis are factors that prevent the mobility of this part of the intestine. Accord-

18. von Haberer, H.: Ulcus duodeni und postoperatives peptisches Jejunalgeschwür, Arch. f. klin. Chir. **109**:413, 1918.

19. Clairmont, P.: Ueber das Vorkommen, die Diagnose und Therapie des Ulcus pepticum jejuni, Verhandl. d. Gesellsch. deutsch. Naturf. u. Aerzte **2**:390, 1913.

20. Schur, H., and Plaschkes, S.: Die Bedeutung der Funktion des Antrum pylori für die Magenchirurgie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **28**:795, 1915.

21. Aschoff, Ludwig: Lectures on Pathology, New York, Paul B. Hoeber, Inc., 1924.

22. Chiari, O. M.: Ueber das postoperative Jejunalulcus, Arch. f. klin. Chir. **134**:709, 1925.

ing to our own opinion, the location of the jejunal ulcers on the anterior wall or the distal loop, along the attachment of the mesentery or even in the proximal loop can be explained on the basis of mechanical factors, since the stomach and intestine are not made of inert, immovable material and vary in their position during the stages of filling and emptying and because of the changes in the intra-abdominal pressure. The method of anastomosis and the chance adhesions will also determine the location of the mechanical insults. It is therefore impossible to predict the exact part of the intestine which will receive the mechanical insult determining the location of the ulcer.

The mechanical factors may be manifold and may depend on the spastic conditions that occur about the anastomotic opening and that have been particularly emphasized by Blond.[23] An incarceration of the

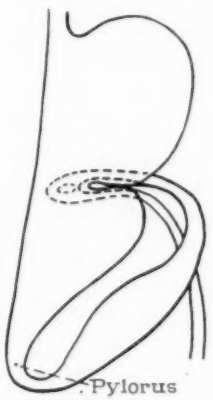


Fig. 1.—Hour-glass spasm within the anastomotic area. The proximal and distal loops of the jejunum are deeply pulled into the gastro-enterostomy opening and are pinched. (From Meyer-Burgdorff, H., and Schmidt, W.: Der Operierte Magen, Leipzig, Georg Thieme, 1930.

jejunum at the anastomotic opening may be caught in the hour-glass contraction of the stomach (fig. 1); there may also take place intermittent invaginations of the jejunum into the gastro-enterostomy opening or circular spasms of the distal loop of the jejunum.

Aside from the spastic condition emphasized by Blond,[23] we believe that the nature of the anastomosis of the intestine to the stomach predisposes to a mechanical spur formation (figs. 2 and 3). This would be the case particularly in the method of anastomosis advocated by

23. Blond, K.: Ueber den sogenannter Circulus vitiosus nach Gastroenteroanastomose, Med. Klin. **17**:1412, 1921; Die Beziehungen des sogenannten Circulus vitiosus nach Gastroenteroanastomose zum Ulcus pepticum jejuni postoperativum; Ein Beitrag zur Spasmogen-Ulcusgenese, Arch. f. klin. Chir. **135**:381, 1925.

Moise,[24] in which a transverse incision is made into the intestine. We have seen such a case lately, post mortem, in which the spur produced an actual obstruction of the opening into the stomach (fig. 3). Blond [25] expressed the opinion that such invaginations would be more frequently found if careful study were made in all cases in which there are functional complaints following gastro-enterostomies.

Nothnagel,[26] Leriche [27] and others observed that these invaginations disappear spontaneously and may also recur. Reischauer [28] expressed the belief that the symptoms of the vicious circle may be attributed to a titanic contraction of the upper loops of the intestine or the whole small intestine, owing to a hypertonic condition of the vagus. Dilatation, alone or combined with hypertrophy of the muscle wall of the distal fragment of the jejunum, has been observed by Steindl,[29] Blond [25]

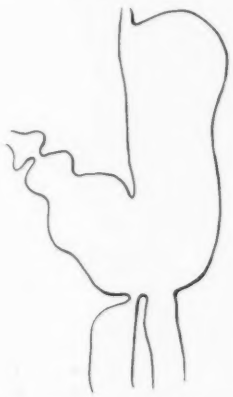

Fig. 2.—A diagrammatic presentation of the duodenal spur following a gastro-enterostomy opening. (From Meyer-Burgdorff and Schmidt.)

and many others. The dilatation distal to the gastro-enterostomy opening is limited more or less sharply and is explained on the basis of a spastic block of the distal fragment. Any one who has operated extensively on the bowel, particularly in dogs, will agree with Winkelbauer,[30] who called attention to anemic spots and contractions of the

24. Moise, T. S.: Gastroenterostomy with a Transverse Jejunal Incision, Surg., Gynec. & Obst. **44**:829, 1927.

25. Denk (footnote 23, first reference).

26. Nothnagel, C. W. H.: Die Erkrankungen des Darms und des Peritoneums: Ulcus duodeni simplex, Vienna, A. Hölder, 1903, vol. 5, p. 173.

27. Leriche, R.: Rev. de chir. **1**:878, 1914.

28. Reischauer, F., quoted by Hertel (footnote 13).

29. Steindl, H.: Neue Gesichtspunkte zum Problem des Enterospasmus, Arch. f. klin. Chir. **139**:245, 1926.

30. Winkelbauer, A.: Studien über die Verhütung des Ulcus pepticum postoperativum im Experiment, Arch. f. klin. Chir. **143**:649, 1926.

lumen of the small intestine due to irritation or to the introduction of a needle into the intestinal wall. The same observations have been made on various occasions by the senior author in certain irritable stomachs in which the antrum or even the omentum is pinched during an operation. The distal part of the stomach contracts in part or altogether, and this contracted condition has been mistaken for a malignant process. This was particularly true in three of our own cases, in which roentgen examination of the stomach revealed a deformity strongly suggestive of a malignant condition. We are informed of a case in which the antrum was removed by an experi-

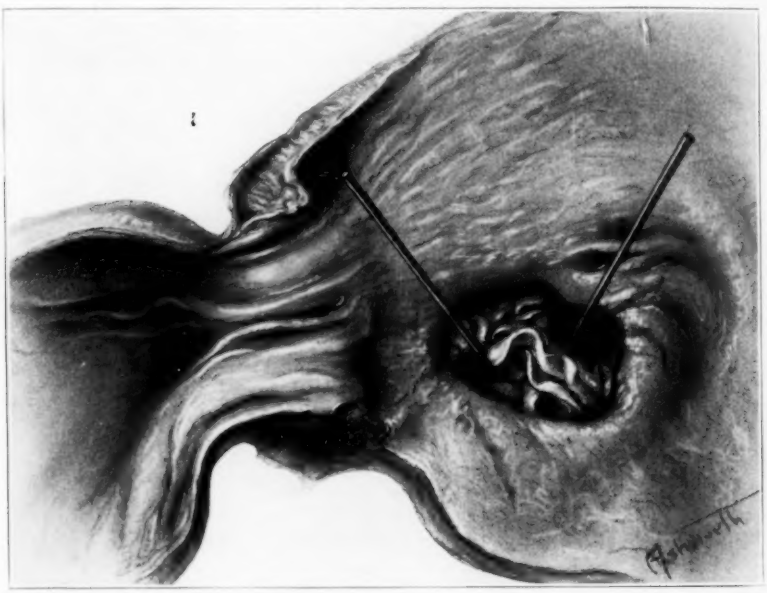

Fig. 3.—A postmortem specimen of a dilated stomach with a gastro-enterostomy demonstrating a spur formation of the jejunum into the lumen of the stomach.

enced surgeon, and a diagnosis of carcinoma was made grossly by the pathologist who was present at the operation. The condition was soon shown to be purely a spasmodic contraction.

The etiology of such jejunal invaginations into the gastro-enterostomy opening is due to local spasms. The anatomic conditions are as favorable here as in the invagination of the movable ileum into the cecum, since the jejunum is movable while the anastomosis is more or less fixed (fig. 3). In this connection we may add our own observations of several animals in which intussusception of the small intestine took place at the site of irritation from an injury of the peritoneal covering or from the presence of worms in the intestine.

It is not always possible to separate the mechanical from the chemical factors influencing the production of peptic ulcers. Kocher [31] believed that peptic ulcer was due to stagnation of the contents of the stomach above a contraction of the jejunum. The healing of an ulcer after perforation into the large bowel might also be explained on the same basis, as due to improved conditions of drainage.

The relation of the spastic condition of the jejunum anastomosed to the stomach to the genesis of postoperative ulcers has also been studied by Winkelbauer.[30] He utilized the method of Kreidel, who demonstrated on dogs that the circular and longitudinal muscle layers can be removed from large areas of the stomach and intestine without any apparent harm to the dog. The mucosa left after the muscle layers have been stripped off is sufficient protection against perforation. This procedure is similar to the Weber-Rammstedt operation for hypertrophic stenosis in infants. Winkelbauer [30] used Exalto's method of implantation of the duodenum into the colon, with the exclusion of a large part of the stomach, after the method of von Eiselsberg. According to Exalto,[11] Winkelbauer [30] and others, this method invariably produces an experimental peptic ulcer. In dogs in which, in addition to the foregoing procedure, he stripped off about 15 or 25 cm. of the muscle area in the distal jejunum anastomosed to the stomach, he obtained no ulcers. This experimental observation is of the greatest importance in pointing out that spastic conditions of the small intestine are directly or immediately related to the etiologic factors in the experimental production of peptic ulcers.

## THE EXPERIMENTAL PROBLEM

As far as we know, no systematic study has been made to determine the direct influence of the motor or mechanical force of the different anatomic and physiologic subdivisions of the stomach on the experimental production of peptic ulcers. The distal part of the stomach, the pars ejestoria, is the motor and the active peristaltic factor in propelling the food. The force with which it ejects the contents of the stomach is more powerful than that in the fundus with its weak musculature. For this reason the narrow pyloric valve anastomosed to the jejunum will eject a smaller stream with a more powerful force than it would if the opening in the pyloric part of the stomach were made larger by removing the sphincter in an oblique line (fig. 10).

Another way of changing the mechanical force with which food is propelled from the stomach is to produce some form of impediment, such as a kink, in the jejunum directly under the anastomosis. Such a

31. Kocher, T.: Demonstration eines Ulcus pepticum jejuni nach Gastroenterostomie, Verhandl. d. deutsch. Gesellsch. f. Chir. **1**:103, 1902.

procedure would directly accentuate the trauma of the propelling force of the stomach against the jejunum and at the same time produce a stagnation of the contents of the stomach above the artificial impediment.

The experimental and clinical methods used in gastro-intestinal anastomosis influence not only the mechanical but also the chemical conditions. In our experimental work we made an attempt to estimate the importance of each of these factors.

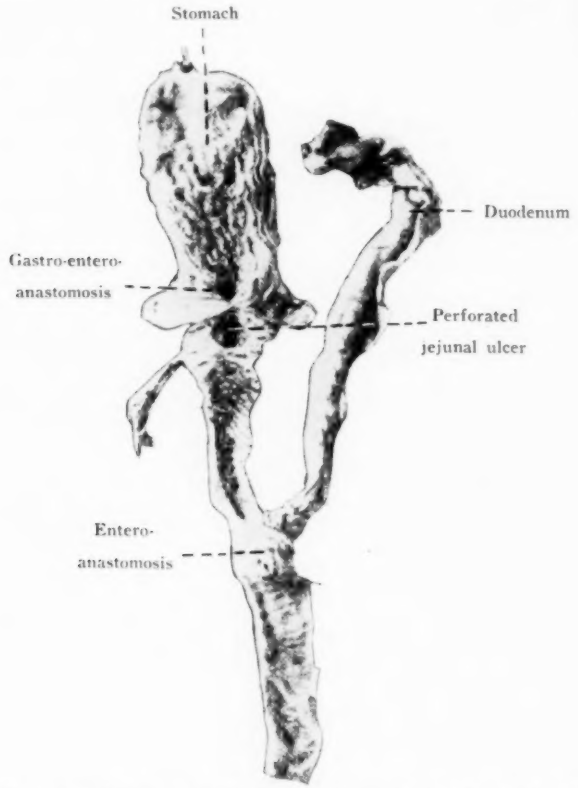


Fig. 4.—Reproduction of the original photograph of Exalto's short-circuiting operation published in 1911. (Exalto, J.: Ulcus jejuni, nach Gastroenterostomie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **23**:13, 1911.)

For some time a standardized technic has been used by many investigators by which the duodenal contents can be diverted to the ileum or to the large intestine by dividing the duodenum either below or just short of the pyloric ring, closing the proximal opening, and implanting the duodenum some distance from the gastro-enterostomy opening. Mann and Williamson [32] published their work utilizing the

32. Mann, F. C., and Williamson, C. S.: The Experimental Production of Peptic Ulcer, Ann. Surg. **77**:409 (April) 1923.

same principal that Exalto [11] used in 1911 (fig. 4). Several of Mann's co-workers, and Mann himself, have emphasized this particular procedure and choose to call it Mann's original method of "surgical duodenal drainage." McCann [33] published an extensive study of experimental peptic ulcers from Mann's laboratory. In this otherwise commendable work he misquoted the figures and results of Exalto's experiments. McCann [33] stated that Exalto "observed jejunal ulcers, often multiple, in six of ten dogs operated on in this manner." As a matter of fact, Exalto [11] operated on fourteen dogs; in seven dogs he performed a gastro-enterostomy with exclusion according to von Eiselsberg, but obtained no ulcers. In four dogs he performed an exclusion operation with a "Y" anastomosis of Roux, and was able to observe three ulcers. In the last three experiments he used the same procedure except that he implanted the distal part of the duodenum into the colon. In these last three experiments he observed an ulcer in every case. In addition to the foregoing experimental procedures, he fed all the dogs, with the exception of the last one, given amounts of hydrochloric acid.

McCann [33] also quoted to the effect that "Exalto performed gastro-enterostomy after excluding the pylorus; he then drained the duodenal alkalis of the proximal loop into the cecum." However, McCann failed to mention that the method Exalto used is the same as that of Mann, with the slight difference that in Exalto's experiments the division was made immediately above the pylorus, while in Mann's experiments the division was made immediately beyond the pylorus. Since Exalto [11] published his method in 1911 (fig. 4) and obtained results later verified by Mann and others, and since Exalto's method has been used by many experimental workers and considered as a standard technic, we believe that priority is due to Exalto, and that he should receive credit for the originality of this technic. It is also our opinion that the term "surgical duodenal drainage" does not describe this procedure as well as "the short-circuiting of the duodenal contents." A reproduction of Exalto's original photograph of his operation is given in figure 4.

### COMMENT ON THE EXPERIMENTAL DATA

One hundred dogs were used in these experiments; some of the animals died soon after the operation. If the findings were negative to ulcer formation, the animals were not included in our statistics, since two or three days, or even a week, is too short a time to allow deductions in the absence of ulcers; on the other hand, if the dogs died a few days after the operation from peritonitis or hemorrhage due to an acute perforated ulcer, this was naturally considered as positive experimental evidence of ulcer formation.

33. McCann, J. C.: Experimental Peptic Ulcer, Arch. Surg. **19**:600 (Oct.) 1929.

We performed various types of gastro-intestinal anastomosis and also diverted the alkaline duodenal contents distal to the anastomosis according to the short-circuiting method of Exalto (fig. 4). At the beginning of our experiments both of these operations were performed at one stage, but later, when it was possible, the gastro-intestinal anastomosis was performed first and the short-circuiting operation at a later date. The two-stage operation gave us an opportunity to study the simple gastro-intestinal anastomosis without short-circuiting the duodenal contents. These operations therefore served as control experiments. Exalto,[11] Mann and Williamson [32] and others short-circuited the duodenal contents into the terminal ileum or the large bowel. This produces a tremendous disturbance in the physiology of the intestinal tract of the animal, which lowers its resistance, and in

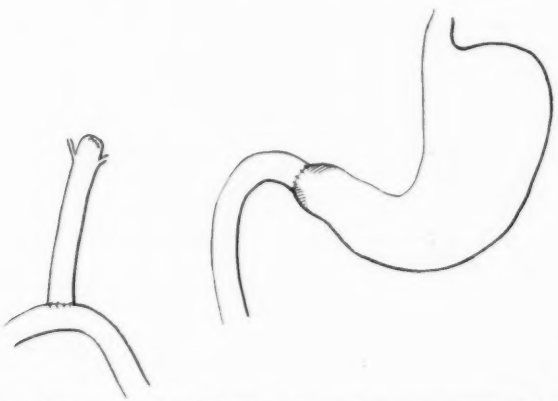

Fig. 5.—The diagram on the left shows an end-to-end gastroduodenal anastomosis with the pylorus left intact; that on the right, Exalto's short-circuiting operation.

itself is sufficient to influence the production of peptic ulcer. On account of these considerations, we implanted the distal end of the duodenum about 60 cm. from the gastro-intestinal anastomosis, allowing the bile and pancreatic juice enough of the mucosa of the area of the small intestine for the performance of their functions.

### END-TO-END ANASTOMOSIS BETWEEN THE PYLORUS AND THE JEJUNUM WITH SHORT-CIRCUITING OF THE DUODENAL CONTENTS (FIG. 5)

Seven dogs were operated on in this manner. Ulcers developed in all of the animals; in five acute perforated ulcers developed from five to sixteen days after the operation, and death was due to either peritonitis or hemorrhage. One dog died on the fifth postoperative day, revealing an area of inflammation in the jejunum in a line with the lesser curvature of the stomach. The inflammatory area was 10 cm.

long and was covered by a diphtheritic membrane. One dog was killed on the sixty-ninth day, and a chronic indurated ulcer was found on the jejunum (fig. 6). The ulcer was 1 cm. from the gastro-intestinal anastomosis, situated on the anterior aspect of the jejunum in a line with the lesser curvature of the stomach.

These experiments demonstrate conclusively that when the alkaline duodenal contents are diverted from the end-to-end gastro-intestinal anastomosis, with the pyloric ring left intact, an ulcer develops in 100 per cent of the experiments. When we compare these results with those in which some other methods of gastro-intestinal anastomosis have been used, with less uniform results, we must naturally allow for

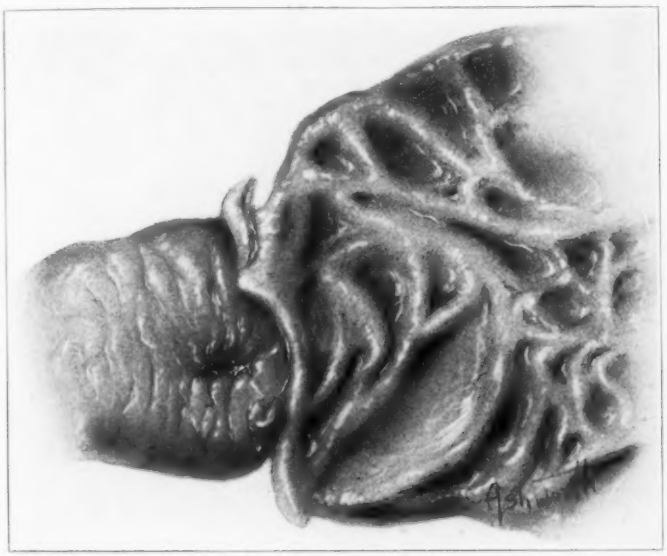

Fig. 6.—A small chronic ulcer in the jejunum following an end-to-end anastomosis between the stomach and the jejunum, and an Exalto short-circuiting operation.

additional factors contributing to the formation and chronicity of these ulcers.

The pars pylorica, which is the motor part of the stomach, possesses a thick muscle wall; it engages in active peristaltic movements and propels the contents of the stomach forcibly through a narrow pyloric ring into the jejunum, which is anastomosed end-to-end. Digestion of the jejunal mucosa would be expected at the place where the acid chyme constantly strikes the mucosa and produces a rather localized mechanical and chemical trauma. The location would depend not only on the method of anastomosis but on the chance position the jejunum may assume due to adhesions and other factors not under the surgeon's control.

In two animals the ulcers were on the anterior jejunal wall; in two others they were on the posterior and anterior jejunal walls, and in three dogs the ulcers were on the jejunal side on a line with the lesser curvature of the stomach.

It is quite possible that more chyme strikes that part of the jejunum which is directly anastomosed to the terminal part of the lesser curvature than any other part. The function of the lesser curvature has been elaborated, particularly by Aschoff.[21]

In one animal, not included in the foregoing experiments, an obstructive jaundice developed from obstruction of the common duct due to invagination of the proximal closed end of the duodenum. It died three days after the operation from hemorrhage due to numerous erosions of the mucosa of the stomach (fig. 8). This demonstrates that in experimentally produced obstructive jaundice, in the presence

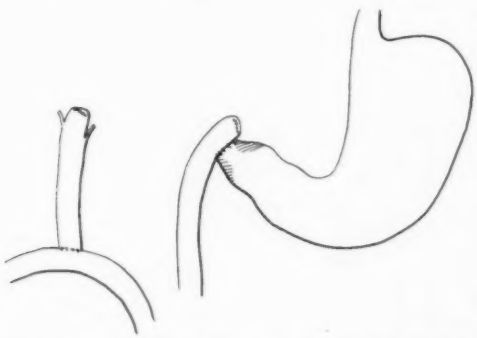

Fig. 7.—The diagram on the left shows an end-to-side gastrojejunal anastomosis with the pylorus left intact; that on the right, Exalto's short-circuiting operation.

of the Exalto short-circuiting operation, when the acid values of the stomach are high, erosions may form and cause a fatal hemorrhage.

### TERMINOLATERAL GASTRO-INTESTINAL ANASTOMOSIS WITH THE PYLORUS LEFT INTACT (FIG. 7)

In this series of experiments the usual Exalto short-circuiting operation was performed, the distal end of the duodenum being implanted into the small intestine about 60 cm. from the pylorus. The pylorus was then anastomosed to the jejunum end-to-side. Of the animals operated on in this manner, seven have survived long enough to enable us to draw certain conclusions. In three dogs typical chronic ulcers developed in the jejunum. The observation of these animals lasted from four to ninety days. In one dog perforated ulcer developed on the posterior wall of the jejunum next to the anastomosis, and it died seven days after the operation. One dog was killed at the end of fifty-seven days and another at the end of sixty-seven days, and no ulcers were found.

This form of anastomosis produced ulcers in only about 43 per cent of our experiments, and most of the ulcers were chronic. The locations of the ulcers were opposite the opening of the pylorus, corresponding to the lesser curvature of the stomach (fig. 9). The chronicity of the ulcers in these cases, in contradistinction to the acute perforating type in the end-to-end anastomosis, can be attributed to the fact that

Fig. 8.—Erosions of the mucosa of the stomach following Exalto's short-circuiting operation and an end-to-end anastomosis between the stomach and the jejunum, with accidental obstructive jaundice.

an end-to-side anastomosis allows much more room for the impact of the chyme of the stomach from the pyloric opening. The location of the ulcers opposite the pyloric opening is evidently due to trauma, since in the end-to-side anastomosis the relative position between the opening in the stomach and the jejunum can be more easily controlled (fig. 7).

As explained, the position of the proximal jejunal wall in the end-to-end anastomosis is more capricious, and the location of the ulcer will vary according to the position of the jejunum. On account of the weight of the distal jejunal loop, the anterior wall of the jejunum will be closer to the opening of the pylorus (fig. 5).

An additional factor influencing the production of experimental ulcers is to be found in the degree of acidity and in the emptying time of the contents of the stomach. The lumen of the dog's jejunum is quite narrow, and the end-to-end anastomosis between the latter and

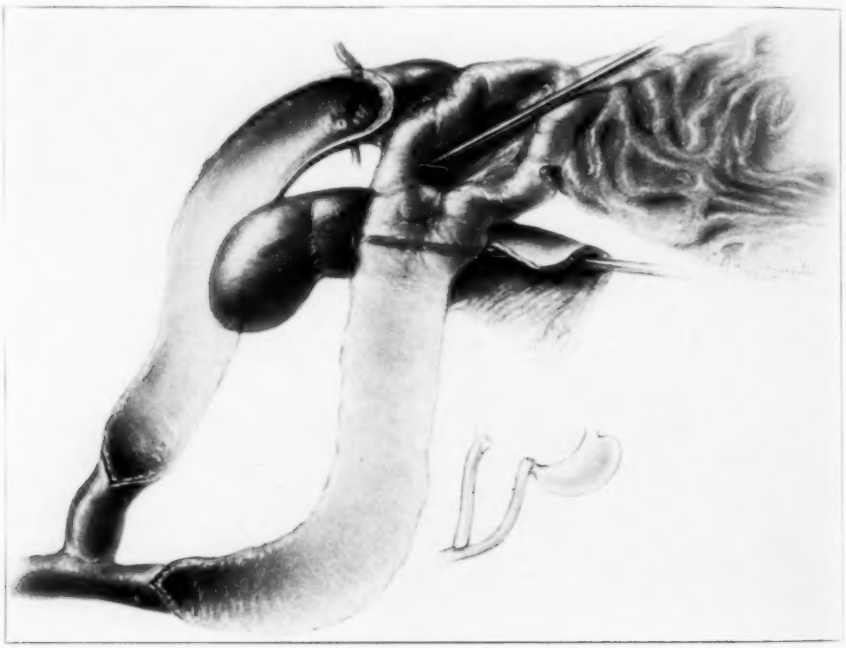

Fig. 9.—A large, chronic, indurated ulcer in the jejunum perforated into the appendix following an end-to-end anastomosis, with the pylorus left intact, and the usual Exalto short-circuiting operation.

the pylorus will shrink and become much narrower than the opening in the end-to-side anastomosis. For this reason the emptying time will be delayed and the degree of acidity will be higher in the end-to-end anastomosis. This was actually demonstrated in chemical examination in the various types of operations on the stomach. (Some of the chemical studies are to be published at a later date.)

### TERMINOLATERAL JEJUNAL ANASTOMOSIS WITH A MINIMUM PART OF THE PYLORUS OF THE STOMACH REMOVED (FIG. 10)

In these experiments we attempted to change the mechanical and chemical factors. The usual Exalto short-circuiting operation was

performed, the alkaline contents of the duodenum being diverted from the gastro-intestinal anastomosis. The distal 2 cm. of the pyloric portion of the stomach, including the pyloric valve, was removed. The incision into the stomach was made in an oblique line from the lesser curvature on the right side to the greater curvature to the left (fig. 10). In this manner the terminolateral anastomosis was made wide without sacrificing too much of the stomach. This procedure not only enlarged the gastro-intestinal anastomosis, but also partially paralyzed the propelling force of the stomach by removing a part of its motor pyloric end. The emptying time of the contents of the stomach in this operation is more rapid than in the previous methods of anastomosis, and the degree of acidity is lower.

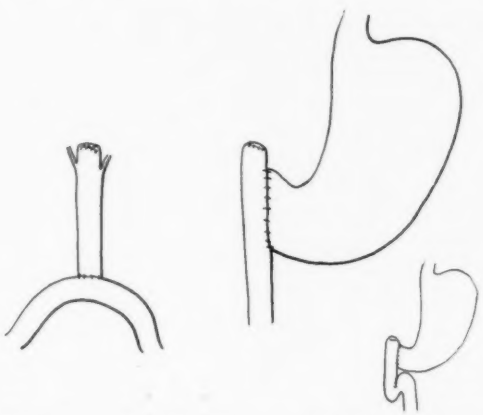

Fig. 10. The diagram on the left shows an end-to-side gastrojejunal anastomosis, with a minimal part of the pylorus removed; that in the center, Exalto's short-circuiting operation, and that on the right, a kink 5 cm. distal to the anastomosis.

Of these animals, sixteen have survived long enough to demonstrate the effect of this surgical procedure on ulcer formation. All of the animals were alive for from thirty-two to seventy-five days. Most of them were operated on in two stages. Chronic jejunal ulcers developed in only two dogs.

In three dogs the jejunum next to the anastomosis was markedly inflamed; eleven dogs showed no evidence of inflammation or ulcers in the period of observation of from thirty-seven to seventy-five days.

This operation, in which only part of the pylorus is removed, throws more light on the factors concerned in the production of experimental peptic ulcers. The partial paralysis of the motor force of the pylorus, the rapid emptying of the contents of the stomach and the lessened degree of acidity have prevented the formation of ulcers in fourteen of sixteen dogs operated on in this manner.

In dog 33 the ulcer was 5 by 1 cm. in diameter and had indurated edges; it was situated on the anterior wall of the jejunum at the proximal end of the anastomosis, again corresponding with the line of the lesser curvature (fig. 11).

Dog 8 was killed on the thirty-second day. Three ulcers of various sizes were found in the jejunum, all on the posterior wall. One was found directly at the anastomosis, another one at the distal part of the anastomosis, and one about 5 cm. from the distal end of the anastomosis (fig. 12). This demonstrates that the location of the ulcers

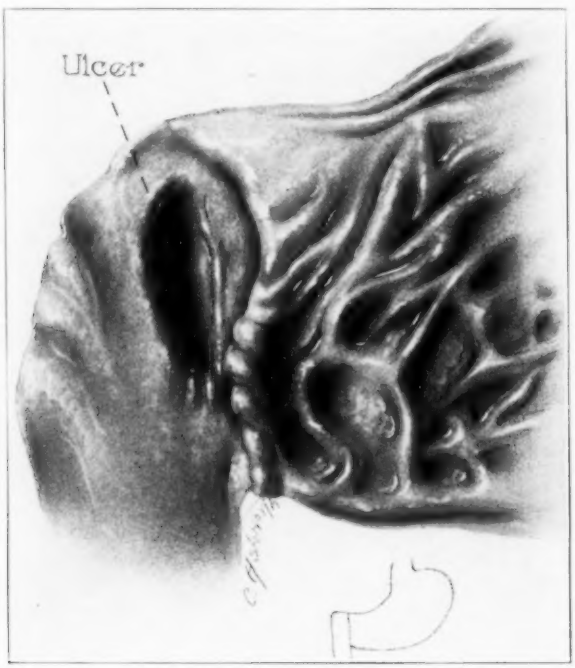


Fig. 11.—A chronic ulcer in the jejunum, with overhanging of the distal edge following an end-to-side gastrojejunal anastomosis with the removal of a minimal part of the pylorus, and an Exalto short-circuiting operation.

may vary, since the factors of mechanical and chemical trauma are not always under experimental control.

Only artificially produced kinks may determine the location of the ulcer (fig. 13).

### SUBTOTAL GASTRIC RESECTION WITH VARIOUS BILLROTH GASTROINTESTINAL ANASTOMOSES AND THE EXALTO SHORT-CIRCUITING OPERATION (FIG. 14)

In the foregoing experiments we have attempted to determine what influence the removal of only a small part of the motor part of the

stomach has on the formation of jejunal ulcers. In the series to be described we have proceeded with the resection of more than the distal muscular part, leaving only the proximal one-third. The remaining part of the stomach has the function of active secretion of gastric juice, and exhibits only tonic contractions. As in all our previous experiments, we have in this instance diverted the alkaline duodenal contents from the gastrojejunal anastomosis, using the short-circuiting method described by Exalto.[11] Twelve anastomoses were performed after the

Fig. 12.—Several acute ulcerations, one perforated, following an end-to-side anastomosis between the stomach and the jejunum, with a minimum part of the pylorus removed, and the usual Exalto short-circuiting operation (*a*).

method of Finsterer-Hoffmeister (fig. 14 *B*), two after the method of Polya (fig. 14 *A*) and six after the Billroth I method modified by von Haberer, in which the large lumen of the stomach was made small in order to enable us to anastomose it end-to-end to the jejunum (fig. 14 *C*). Ulcers developed in none of these animals, with the exception of two of six operated on according to the method of von Haberer. In these two cases the lumen in the gastro-intestinal anastomosis was not

larger than 1 cm. in diameter, and only the distal half of the stomach was removed. All of these dogs were observed for a long period of time—some as long as three months. In analyzing the factors that have prevented the formation of ulcers in the dogs operated on according to the Billroth II method, we wish to call particular attention to the fact that the whole muscular, motor and propelling part of the stomach was removed, and that the anastomosis between the stomach and the

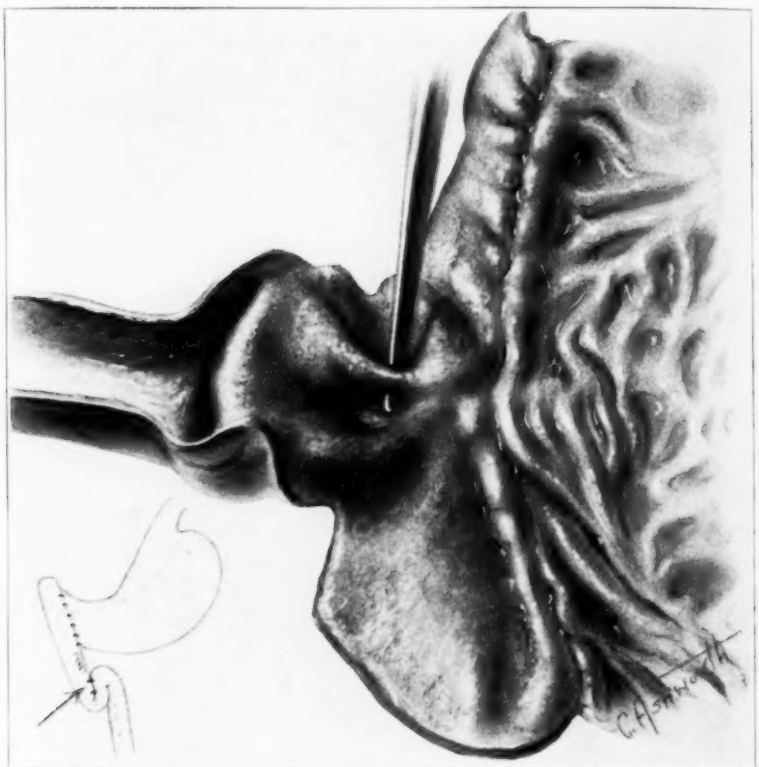

Fig. 13.—An undermined ulcer following an end-to-side anastomosis between the stomach and the jejunum, with a minimal part of the pylorus removed. The ulcer occurred only after a kink was made in the jejunum. The usual Exalto's short-circuiting operation was also performed.

intestine was made wide. Such a procedure eliminates the periodic localized trauma by acid stomach contents against the jejunum and produces a rapid but rather passive emptying of the stomach.

The variation of the chemical factors in this series of experiments should be taken into consideration, since the emptying time is hastened. It should not be forgotten that in removing a larger part

of the stomach than the antrum, some of the acid-secreting fundus glands are also removed. On the other hand, the short-circuiting operation of Exalto removes the bile and pancreatic juice, and therefore the reaction of the contents of the stomach, in spite of the large resection, is never completely anacid (Steinberg, Brougher and Vidgoff [17]).

Evidence that the mechanical factors, in the presence of unneutralized acid pepsin, influence the formation of ulcer can be substantiated by two of this series of experiments, in which a modified von Haberer anastomosis was performed with a narrow lumen and the removal of

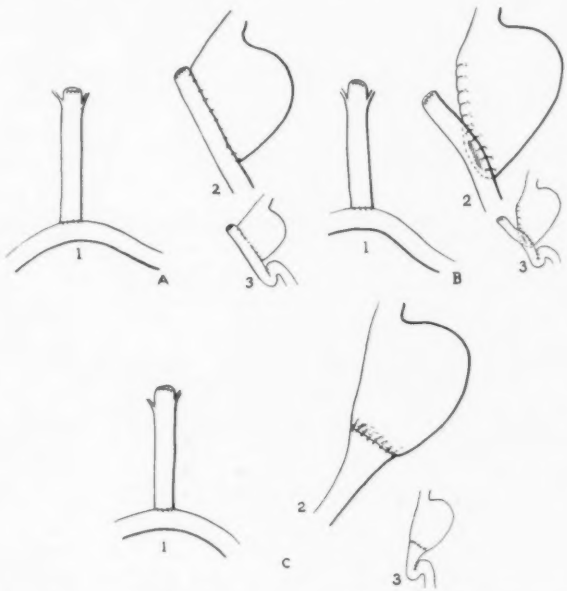


Fig. 14.—In *A*, *1* shows a subtotal resection of the stomach according to the method of Billroth II modified by Polya; *2*, Exalto's short-circuiting operation; *3*, a kink made 5 cm. distal to the anastomosis. In *B*, *1* shows a Billroth II resection of the stomach modified by Finsterer; two thirds of the stomach was removed; *2*, Exalto's short-circuiting operation diverting the alkaline duodenal contents distal to the anastomosis; *3*, a kink 5 cm. distal to the anastomosis. In *C*, *1* shows a subtotal resection of the stomach according to the Billroth I method modified by Haberer; *2*, Exalto's short-circuiting operation; *3*, a kink 5 cm. distal to the anastomosis. The gastro-intestinal stoma is actually much smaller than is presented in this diagram.

a smaller part of the stomach. A small ulcer developed in the jejunum in two of the six dogs operated on according to this method (fig. 15). In the end-to-end anastomoses according to von Haberer, the narrow lumen also tends to retard the emptying time of the stomach, and there-

TABLE 1.—*Summary of the Various Experimental Procedures*

| Type of Operation | Number of Operations | Number of Ulcers | Percentage of Ulcers | Comment |
|---|---|---|---|---|
| Control experiments, including various types of gastro-intestinal anastomoses with the Exalto short-circuiting operation left out | 30 | 0 | 0 | |
| Kink in the duodenum distal to the pylorus | 2 | 0 | 0 | Duodenal mucosa inflamed in one dog |
| End-to-end anastomosis between the jejunum and the stomach with the pylorus left intact and with Exalto's short-circuiting operation, see figure 5 | 7 | 7 | 100 | One dog developed jaundice and died from hemorrhage due to erosions of the gastric mucosa |
| End-to-side anastomosis between the stomach and jejunum with the pylorus left intact and an Exalto short-circuiting operation; see figure 7 | 7 | 3 | 43 | |
| End-to-side anastomosis between the stomach and the jejunum with the pylorus left intact and Exalto's short-circuiting operation; a kink was made in the jejunum 5 cm. distal to the anastomosis | 1 | 1 | 100 | |
| End-to-side anastomosis between the stomach and the jejunum with a minimal part of the pylorus removed and an Exalto short-circuiting operation; see figure 10 | 16 | 2 | 12.5 | In three dogs the jejunum was markedly inflamed |
| End-to-side anastomosis between the stomach and jejunum with a minimal part of the pylorus removed; a kink 5 cm. distal to the anastomosis, and Exalto's short-circuiting operation | 3 | 3 | 100 | |
| Anastomosis between the stomach and the jejunum with a resection of one half of the stomach; a Billroth I method, end-to-end modified by von Haberer, and an Exalto short-circuiting operation; see figure 14 C | 6 | 2 | 33 | This is not a true von Haberer type of Billroth I, since the stomach is anastomosed to the jejunum end-to-end |
| Anastomosis between the stomach and the jejunum with a resection of one half of the stomach; a Billroth I method, end-to-end modified by von Haberer, and an Exalto short-circuiting operation; a kink made 5 cm. distal to the gastro-intestinal anastomosis; see figure 14 C | 4 | 2 | 50 | This is not a true von Haberer type of Billroth I, since the stomach is anastomosed to the jejunum end-to-end |
| A subtotal resection of the stomach and an anastomosis between the stomach and the jejunum, end-to-side, according to the Billroth II modified by Finsterer-Hoffmeister and an Exalto short-circuiting operation; see figure 14 A and B; two Polya included | 14 | 0 | 0 | |
| A subtotal resection of the stomach and an anastomosis between the stomach and the jejunum, end-to-side, according to the Billroth II modified by Finsterer-Hoffmeister and an Exalto short-circuiting operation; a kink made 5 cm. distal to the gastro-intestinal anastomosis; see figure 14 B | 6 | 0 | 0 | |

fore, the acidity of the contents of the stomach is maintained at a high level (table 2).

The mechanical and chemical factors cannot be easily separated, since one may influence the other. These interrelations will be demonstrated in other experiments, which are to follow immediately, and in more chemical examinations made during the course of experiments, which will be published at a later date.

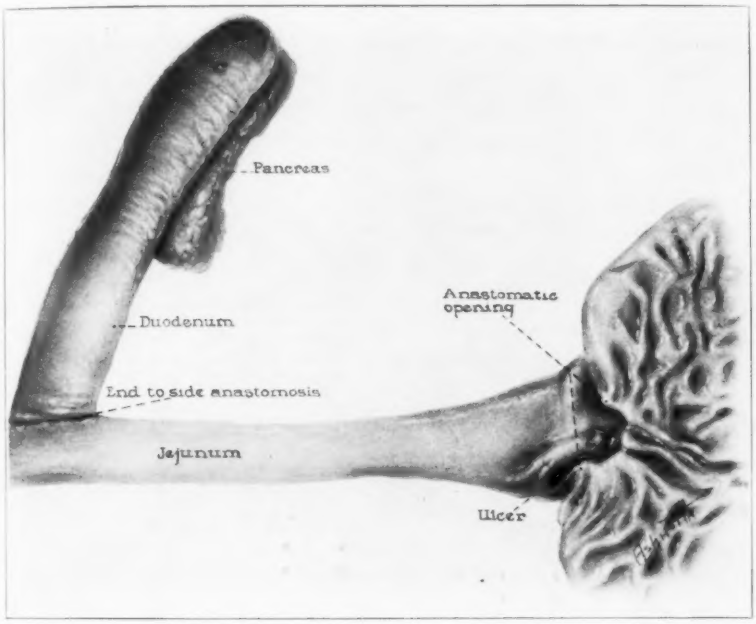


Fig. 15.—A small chronic ulcer in the jejunum about 2 cm. from the termination of the lesser curvature. The Billroth I method of end-to-end anastomosis modified by Haberer was used, the distal half of the stomach being removed.

## PARTIAL OBSTRUCTION AS A FACTOR IN THE ETIOLOGY OF PEPTIC ULCER

In the last few months of our work we introduced new factors to throw more light on the genesis of the postoperative, experimentally produced ulcers. In some of the animals in which ulcers did not develop during the various operative procedures used, we performed a kinking in the intestine 5 cm. distal to the gastro-intestinal anastomosis. Such a procedure can produce an actual mechanical impediment against a forcible ejection of acid chyme, causing it to stagnate for variable periods of time. It was thought that the results of such a partial obstruction would help us greatly in analyzing the various mechanical and chemical factors on the part of the stomach and jejunum. All the

dogs operated on in this manner, with the exception of two controls, had undergone the Exalto short-circuiting of the alkaline duodenal contents. In two animals the anatomic relations of the stomach and duodenum were left intact, and the duodenum was kinked about 5 cm. distal to the pylorus. One dog was killed at the end of nine days and the other at the end of forty-six days. No definite ulcers were seen, except that in a dog that was observed nine days there was a small reddened area about 1 cm. in diameter on the posterior wall of the duodenum proximal to the kink.

One animal that had undergone terminolateral anastomosis between the stomach and the jejunum (the pylorus was left intact) and the Exalto short-circuiting operation was explored at the end of sixty-seven days, and no evidence of ulcer was found (fig. 7). A kink

TABLE 2.—*Chemical Studies of the Stomach Contents After Various Gastro-Intestinal Anastomoses* *

| Dog 85 | | | Dog 66 | | |
|---|---|---|---|---|---|
| Billroth II method modified by Finsterer—wide stroma (fig. 14 B) | | | End-to-end anastomosis between stomach and jejunum, modified after von Haberer's method of Billroth I—narrow stroma (fig. 14 C) | | |
| Meal given at 4 p. m. | | | Meal given at 8 p. m. | | |
| Time of Examination | Free Acidity | Total Acidity | Time of Examination | Free Acidity | Total Acidity |
| 4:15 | 0.0000 | 0.0273 | 8:15 | 0.0000 | 0.0729 |
| 4:30 | 0.0000 | 0.0273 | 8:30 | 0.0000 | 0.0820 |
| 4:45 | 0.0000 | 0.0456 | 8:45 | 0.0456 | 0.1459 |
| 5:00 | 0.0000 | 0.0456 | 9:00 | 0.1003 | 0.2918 |
| 5:15 | 0.0000 | 0.0364 | 9:15 | 0.1094 | 0.3007 |
| 5:30 | Stomach empty | | 9:30 | Stomach empty | |

* The test meal consisted of 50 Gm. of hamburger steak brought to a boil in 300 cc. of water.

was made 5 cm. distal to the anastomosis between the stomach and the jejunum. This animal died five days after the partial obstruction was created, from peritonitis due to a perforated ulcer proximal to the kink.

Three dogs that had undergone a minimum resection of the pylorus with an end-to-side anastomosis between the stomach and the jejunum and also an Exalto short-circuiting operation were observed for a period of from thirty-seven to seventy days (fig. 10). These three dogs were explored, and no ulcers were found. A kink was made in all of the animals 5 cm. distal to the terminolateral anastomosis (fig. 13). In each one of these animals ulcers developed in the jejunum. Dog 60 was examined seventy days after the kink was made, and an indurated scar was found at the jejunum next to the greater curvature of the stomach. Dog 38 was killed forty days after the kink was made, and a small ulcer 5 by 7 mm., with indurated edges, was found on the posterior surface of the jejunum just proximal to the kink. In dog 43

acute peritonitis developed seven days after the kink was made. The exploratory incision in the wall of the stomach gave way; an ulcer 1 cm. in diameter just proximal to the kink was found.

The animals that were subjected to subtotal gastric resection, four according to the Billroth I, end-to-end method, modified by von Haberer (fig. 14 *C*), and six according to the Billroth II method, modified by Finsterer (fig. 14 *B*), with an Exalto short-circuiting operation, were explored after two or three months of observation, and no evidences of ulceration were found. We performed a kink in each one of these animals 5 cm. distal to the gastro-intestinal anastomosis. The animals were observed from twenty-seven to sixty days and then killed. In two dogs operated on according to the Billroth I, end-to-end method, modified by von Haberer, ulcers developed (figs. 14 *C* and 15).

Though these experiments are not numerous, yet they demonstrate definitely the importance of certain indisputable facts. When the muscular, pyloric part of the stomach was left intact, or partially removed, and a terminolateral anastomosis was performed, together with an Exalto short-circuiting operation, and when no ulcers were found, ulcers developed in all the dogs when an impediment to the flow of the acid chyme was made in the form of a partial obstruction. On the other extreme is the absence of ulcers in subtotal resection with a Billroth II anastomosis, an Exalto short-circuiting operation and a kinking. Again, the factors concerned in these experiments are evidently the propelling of the acid chyme by the muscular pylorus with a certain force against an impediment distal to the anastomosis. How much the stagnation of the acid chyme is responsible for the ulcer formation is difficult to estimate. The striking fact that no ulcers were present in any of the animals subjected to subtotal gastrectomies according to the Billroth II method again supports the view that it is in part the absence of the *vis a tergo* of the pyloric part of the stomach which is responsible for the lack of ulcer formation in the dogs on which subtotal resection is performed. It is true, as mentioned, that after a subtotal gastrectomy according to the Billroth II method a part of the actual acid-secreting area of the stomach is also removed, and the rapid emptying time reduces the acidity of the contents of the stomach.

### CONTROL EXPERIMENTS

Our belief that chemical and mechanical factors are primarily responsible for the formation of experimental peptic ulcer is supported by the control experiments in which we performed the various forms of gastro-intestinal anastomosis, leaving out the Exalto short-circuiting operation. This allowed the alkaline duodenal contents the opportunity to neutralize the acid contents at the site of gastro-intestinal anastomosis.

There were thirty dogs in this series; they were observed for a period of from nineteen to sixty days. None of them showed any evidence of ulcer formation. As soon, however, as the Exalto short-circuiting operation was performed, in some of the dogs, ulcer formation took place.

## COMMENT

The factors concerned in the etiology of the experimentally produced, postoperative peptic ulcers have been discussed in a review of the literature and in the protocols of our experiments. It remains only to crystalize and coordinate the accumulated data.

Thirty control experiments with the various gastro-intestinal anastomoses have not yielded a single ulcer. It was only when the gastro-intestinal anastomosis was subjected to the acid gastric contents, which were prevented from being mixed with the alkaline duodenal contents, that peptic ulcer occurred. It is therefore quite evident that acid pepsin is of the greatest importance in the causation of the experimentally produced ulcer. The mechanical factors are somewhat more difficult to analyze, since the various operations on the stomach bring about some change in the acidity of its contents. There were, however, two types of experiments in which we did not expect much change in the chemical factors, while the forms of gastro-intestinal anastomoses were different. In the end-to-end anastomosis between the stomach and the jejunum, with the Exalto short-circuiting operation, ulceration developed in all the animals (fig. 5), while in the end-to-side anastomosis they developed in only 43 per cent (fig. 7). It is therefore the direction of the jejunum and the method of anastomosis which furnish the evidence of the mechanical factor. In the end-to-end anastomosis it is possible that the weight of the jejunum brings its anterior wall closer to the pyloric opening than in the end-to-side anastomosis. Another factor to be considered is the blood supply, which is less disturbed in the end-to-side anastomosis.

When only a minimum part of the pyloric end of the stomach was removed, definite ulcers developed in only two of sixteen dogs. In this particular series of experiments it is difficult to separate the chemical from the mechanical factors and to evaluate each accordingly. It has, however, been demonstrated (Steinberg, Brougher and Vidgoff [17]) that after resection of the stomach in which there is also an Exalto short-circuiting operation the contents of the stomach remain acid. The lack of uniform ulcer formation in this form of anastomosis can be explained by the size of the opening of the stomach, which is wider, and the partial paralysis of the propelling force of the pyloric end of the stomach, which has been partly removed. The traumatic factor has therefore been minimized by this procedure and only after a kink was produced 5 cm. distal to the gastro-intestinal opening did ulceration take

place in each dog so operated on. The additional chemical and mechanical factors in this operation were therefore in the intestine, where an actual partial impediment to the flow of the gastric contents enhanced the trauma and also produced a stagnation of the acid contents.

In two of six animals operated on according to the Billroth I, end-to-end method, modified by von Haberer, ulceration developed in the jejunum (figs. 14 *C* and 15). This was considered as important evidence of mechanical and chemical factors, since the gastro-intestinal opening was very narrow, causing a delayed emptying and a higher acidity of the contents of the stomach (table 2). The absence of ulcers in the series of experiments with the Billroth II method of anastomosis is evidently due to the lack of *vis a tergo* of the stomach, since its muscular pyloric part has been removed. The additional factors considered are the reduced areas of acid-secreting glands which take place in a wide gastro-intestinal anastomosis after a subtotal resection of the stomach.

We have emphasized the traumatic, mechanical and chemical factors in ulcer formation and have taken into consideration the motor drive of the pyloric end of the stomach, the artificial impediment in the jejunum and the width of the anastomotic opening. The invagination of the jejunum into the stomach, which Blond considered as important in the traumatic theory of postoperative ulcer formation, could not have taken place in our experiments with the pylorus intact, since the jejunum could not have invaginated into such a small opening. On the other hand, if the jejunum did invaginate, in our experiments with subtotal resection of the stomach according to the Billroth II method, it was not evidently of great importance, since no ulcers took place in this series of operations. It was impossible in our experiments to evaluate the spasms of the jejunum as of etiologic importance.

The postoperative jejunal ulcers reported following resection of the stomach in the human subject do not evidently correspond to the absence of such ulcers in the dog, in spite of the artificially heightened acidity of the contents of the stomach. This could perhaps be explained by the inherent susceptibility of the human being to ulcer formation. In spite of the difference in the susceptibility of man and the dog to ulcer formation, our experimental work nevertheless emphasized certain factors that will tend to prevent jejunal ulcers in man. The Roux method of anastomosis, either with a gastro-enterostomy or with a subtotal resection of the stomach, diverts the alkaline duodenal contents from the gastro-intestinal opening and influences the formation of postoperative peptic ulcer. After eight subtotal resections of the stomach with the Roux anastomosis, Finsterer (personal communication) reported that post-operative jejunal ulcers developed in seven patients. Finsterer succeeded in curing these patients with jejunal ulcers only after he undid the Roux

anastomosis and restored some of the wall of the stomach. The same argument can be put forward for the lateral entero-anastomosis, which is used to prevent stasis in the proximal loop. The intention of this operation, as in the Roux operation, is to drain the alkaline duodenal contents away from the gastro-anastomotic opening. The reason, however, that the Roux anastomosis and the entero-anastomosis do not give a higher percentage of jejunal ulcers is due to the fact that in spite of the intention of the surgeon to divert the alkaline duodenal contents away from the gastro-anastomotic opening, bile and pancreatic juice find their way into the stomach. The absence of frequent jejunal ulcers after a subtotal resection of the stomach with anticholic anastomosis and the lateral entero-anastomosis may be explained, in addition to the already mentioned factors, also on the basis of the removal of a larger acid-secreting area. The latest statistics (Starlinger [8]) report that the Billroth II resection of the stomach gives 0.6 per cent of jejunal ulcers. From our experimental evidence it would seem that the removal of a large part of the stomach not only causes a low acidity of the stomach contents, owing to the rapid emptying and regurgitation of the alkaline duodenal contents and the actual reduced area of acid-secreting stomach, but also does away with a large part of the stomach with its motor-propelling force. Our experiments would also emphasize that the avoidance of kinks distal to the gastro-anastomosis opening and a wider gastro-intestinal anastomosis will be of some prophylactic value in preventing postoperative jejunal ulcers.

## SUMMARY

One hundred dogs were subjected to various methods of gastro-intestinal anastomosis in order to study the etiologic factors responsible for the formation of postoperative peptic ulcer.

The acid gastric juice of the stomach was prevented from being neutralized by the alkaline duodenal contents by using the short-circuiting operation of Exalto. Exalto, Mann and Williamson and others short-circuited the duodenal contents into the terminal ileum or the large bowel. This produces a tremendous disturbance in the physiology of the intestinal tract of the animal, which lowers its resistance and in itself is sufficient to influence the production of peptic ulcer. On account of these considerations we implanted the distal end of the duodenum about 60 cm. from the gastro-intestinal anastomosis, allowing the bile and pancreatic juice enough of the mucosa of the small intestine area for the performance of their functions.

It was demonstrated that the corrosive action of the acid pepsin in the presence of certain mechanical factors produces peptic ulcerations.

The muscular pyloric part of the stomach propelling the acid contents of the stomach through the pyloric opening may be responsible for the actual localized trauma of the jejunum.

An impediment in the form of a kink in the distal loop of the jejunum or a narrow gastro-intestinal opening favors the development of a jejunal ulcer. These procedures cause a delay in the emptying time and an increased acidity in the contents of the stomach.

Ulcers found immediately in front of a kink also demonstrate that there is a direct mechanical trauma determining the location of the ulcer.

It was conclusively demonstrated that a subtotal resection of the stomach with a wide stoma, performed according to the Billroth II method (Finsterer-Hoffmeister), has never been followed by a peptic ulcer, in our experiments, even in the presence of an artificial kink in the jejunum. This we consider of scientific and clinical interest and importance. On the other hand, the Billroth I method of anastomosis, end-to-end, and the minimal resection of the stomach according to the Billroth II method have given rise to jejunal ulcers, particularly when artificial kinks have been added where no ulcers were originally found. There is, nevertheless, a difference between the experimental method of Billroth I anastomosis, end-to-end, modified by von Haberer, as used in our investigations and the one used in the clinic. In the experimental method the stomach is anastomosed to the very narrow jejunum of the dog, while in the clinical application the stomach is joined to a wider duodenum end-to-end. This will explain the good results obtained by von Haberer in his modified Billroth I method of resection of the stomach.

Only a few of the methods practiced in the surgical treatment for gastroduodenal ulcers were used in our experiments. It is therefore possible that there are variations of the chemical and mechanical factors in other operative procedures, or even in the procedures we used in dogs when applied to the human subject. In this connection we might mention Blond's theory of the invagination of the jejunum into the gastro-intestinal opening, also the spasm of the jejunum. Variation in the predisposition of the subject based on the neurogenic theories that may influence the degree of the psychic secretion and motility of the gastro-intestinal tract should also be taken into consideration.

Many of our experimental procedures are used by the surgeon in treating gastroduodenal ulcerations, and we therefore believe that our data emphasize the fact that a large anastomotic opening between the jejunum and the fundus of the stomach is the best method to prevent jejunal ulcerations.

Kinks in the distal jejunum following gastro-anastomoses should be avoided.

In case an end-to-end anastomosis is necessary in resection of the jejunum for jejunal ulcer, the end-to-end anastomosis should not be placed distal to the gastro-anastomosis, because it may produce the same stasis of the gastric contents in the distal jejunum as a kink.

The entero-anastomosis of Braun, and particularly the "Y" anastomosis of Roux, should be avoided, because these methods, particularly the last one, drain the alkaline duodenal contents away from the gastro-anastomosis. If a Roux anastomosis is considered after resection of the jejunum for gastrojejunal ulcer, it should be placed proximal to the gastro-anastomosis.

It is our opinion that infection plays only a secondary rôle, and that unabsorbable material, clamps and hematoma are only casually responsible for the formation of postoperative peptic ulcer.

# EXPERIMENTAL ILEUS

## II. HIGH OBSTRUCTION WITH THE BILIARY, PANCREATIC AND DUODENAL SECRETIONS, ALONG WITH FOOD AND SODIUM CHLORIDE ENTERING THE BOWEL BELOW THE OBSTRUCTED POINT

HILGER PERRY JENKINS, M.D.
CHICAGO

In a previous communication [1] high obstruction in the dog was found to be compatible with life as long as a month if the biliary, pancreatic and duodenal secretions were short-circuited below the point of obstruction. Six animals lived from twelve to thirty-three days, drank water and ate food occasionally, vomited from time to time, lost weight gradually and showed a gradual fall in blood chlorides and a rise in carbon dioxide-combining power and nonprotein nitrogen, which was most marked shortly before death.

This experiment has been modified in the following manner: The biliary, pancreatic and duodenal secretions were short-circuited by the same type of procedures as described in the previous paper, but in addition the bowel below the point of obstruction was brought out through the abdominal wall as a jejunostomy. Through this the animal was fed milk and cream with small amounts of sodium chloride added and in some instances other substances.

### EXPERIMENT

*Technic.*—The dogs were prepared for obstruction by one or two preliminary operations. Morphine-ether anesthesia was used. Most of the animals were operated on in the following sequence: At the first stage an entero-enterostomy was made between the jejunum just beyond the ligament of Treitz and the jejunum 2 or 3 feet (from 60 to 90 cm.) lower down. At the second stage a pylorectomy and anterior gastro-enterostomy were performed, the jejunum just beyond the entero-enterostomy being used. At the third stage the obstruction was produced in the jejunum just above the entero-enterostomy, and the jejunum was sectioned between the entero-enterostomy and the gastro-enterostomy. The distal stump of jejunum just beyond the obstruction and proximal to the entero-enterostomy was brought to the outside as a jejunostomy. (Figure 1 shows a diagram of the operative procedures.) As a result of these procedures the stomach emptied into

From the Department of Surgery, the University of Chicago.

1. Jenkins, H. P.: Experimental Ileus: I. High Obstruction with the Biliary, Pancreatic and Duodenal Secretions Short-Circuited Below the Obstructed Point. Arch. Surg. **19**:1072 (Dec.) 1929.

the short obstructed loop of jejunum, and the biliary, pancreatic and duodenal secretions as well as food and fluids introduced through the jejunostomy emptied into the bowel below the obstruction.

In several dogs the operative procedures were cut down to two stages. Forced feedings of milk and table scraps in addition to the regular kennel diet were necessary to bring the weights of the animals back to normal after the preliminary operations. Animals that did not regain their original weight were discarded. The animals were kept in metabolism cages. During the period of obstruction the weights were recorded daily. Blood was taken for chemical examination about once a week or oftener if the condition of the animal appeared to show marked change. The plasma carbon dioxide-combining power was determined in volumes per hundred cubic centimeters by the Van Slyke method. The total whole blood chlorides were estimated as sodium chloride by Whitehorn's modification of Volhard's technic. The nonprotein nitrogen was determined by Koch and McMeekin's method.

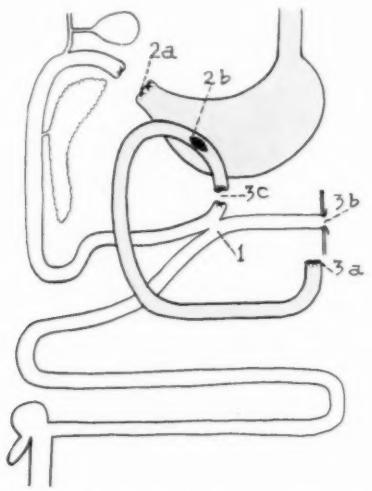


Fig. 1.—Diagram of operative procedures: *1*, entero-enterostomy; *2a*, pylorectomy; *2b*, anterior gastro-enterostomy; *3a*, obstruction; *3b*, jejunostomy, and *3c*, section of jejunum.

The technic of feeding consisted of introducing milk and cream to which an egg was sometimes added into the opening created by the jejunostomy through a catheter connected with a funnel. In some instances other substances were added. The animals appeared to get along better when small amounts were given frequently than when large amounts were given less often. Following the feeding there would frequently be regurgitation of food and digestive secretions from the jejunostomy. This was controlled by inserting a plug into the opening of the bowel. This plug was made by packing a small wad of cotton into the tip of a rubber glove finger. This was fastened to a piece of rolled gauze on the outside which prevented it from slipping down into the bowel farther than the inner side of the abdominal wall. Without this type of plug there was loss of food and also marked digestion of the skin about the jejunostomy from the digestive secretions.

## PROTOCOLS

SERIES I.—*Six dogs operated on first (see Series II), that lived from four to twelve days.*

*Dog 19.*—The weight at the time of obstruction and jejunostomy was 30 Kg. On the first day the jejunostomy was opened, and 1,000 cc. of milk, 50 Gm. of dextrose and 10 Gm. of sodium chloride were given through the jejunostomy in two feedings. This was repeated on the second and third days. Marked diarrhea developed on the third day. The animal became very weak and died on the fourth day. The autopsy revealed no complications. The obstructed part of the jejunum measured 90 cm. and showed no noticeable distention.

*Dog 83.*—The original weight at the time of the obstruction and jejunostomy was 11.2 Kg. On the first day, 250 cc. of milk and cream with two eggs was given. On the following three days 450 cc. of milk and cream with three eggs was given. On the fourth day 2 Gm. of sodium chloride was added to the feedings. Vomiting occurred at least four times. The animal was found dead on the fifth day. At autopsy there was no evidence of complications, and the 23 cm. of obstructed jejunum showed no distention.

TABLE 1.—*Results of Chemical Examination of the Blood of Animals of Series I*

| Dog | Day | Chlorides | Nonprotein Nitrogen | Carbon Dioxide |
|---|---|---|---|---|
| 872 | 0 | 534 | 36 | 48 |
| | 7 | 621 | 31 | 55 |
| | 8 | Death | | |
| 86 | 0 | 424 | 28 | 53 |
| | 7 | 509 | 221 | ? |
| | 7 | Death | | |
| 918 | 0 | 534 | 38 | 43 |
| | 10 | 540 | 37 | ? |
| | 11 | Death | | |
| 942 | 0 | 522 | 23 | 49 |
| | 7 | 603 | 26 | 50 |
| | 12 | Death | | |

*Dog 872.*—When the obstruction and jejunostomy were done, the weight was 11.7 Kg. The animal was given feedings of from 500 to 1,000 cc. of milk with small amounts of sodium chloride daily. The results of chemical examination of the blood on the seventh day were practically the same as before operation (table 1 shows the results for series I). Death occurred on the eighth day. The autopsy revealed no complications. There was no distention of the 55 cm. of obstructed jejunum.

*Dog 86.*—The animal weighed 13 Kg. when the obstruction was produced and the jejunostomy performed. The feedings consisted of from 300 to 500 cc. of milk and cream daily. On the first two days 3 Gm. of sodium chloride was added daily. A bloody diarrhea developed on the fourth day and continued until death occurred on the seventh day. Chemical examination of the blood just before death showed high nonprotein nitrogen and a slight rise in the blood chlorides from 424 to 509 mg. per hundred cubic centimeters. Autopsy revealed no point of hemorrhage in the bowel. The obstructed portion of the bowel was not distended. It measured 25 cm. in length. It was impossible to determine whether the hemorrhage from the bowel was much of a factor in the cause of death. There was no gross evidence of complication.

*Dog 918.*—The animal weighed 23.2 Kg. when the obstruction was produced and the jejunostomy performed. From the second day, from 750 to 1,000 cc. of fluids, consisting of physiologic solution of sodium chloride, milk and dextrose, was given daily in two feedings. Chemical examination of the blood on the tenth day showed practically no change in the chlorides or nonprotein nitrogen. The dog died on the eleventh day, and the postmortem examination showed marked bronchopneumonia, general peritonitis from gangrene and perforation of the loop of bowel brought to the outside as a jejunostomy. The obstructed portion of the bowel measured 40 cm. and was not distended.

*Dog 942.*—When the obstruction was produced and the jejunostomy performed the dog weighed 13 Kg. The daily feedings of 250 cc. of milk and cream with 2 Gm. of sodium chloride were tolerated poorly, because the animal vomited after most of the feedings. Sometimes material that had been put into the opening produced by jejunostomy was vomited. Chemical examination of the blood made on the seventh day showed little change except a slight rise in chlorides. Death occurred on the twelfth day, and at autopsy there was no evidence of a complication. There was, however, reestablishment of a very small lumen of the sectioned jejunum proximal to the site of the gastro-enterostomy. This explained why some of the material injected into the jejunostomy opening appeared in the vomitus. There was no distention of the obstructed portion of the bowel. It is difficult to ascertain whether the reestablishment of a small lumen would appreciably alter the results in this animal. Nevertheless the data on this dog must be considered as possibly atypical even though they fit in with the results that were obtained in the other animals of the series.

SERIES II.—*Five dogs that lived from twenty-one to thirty-seven days.*

*Dog 96.*—During the first week after obstruction and jejunostomy about 500 cc. of 2 per cent sodium chloride was given daily by mouth and practically nothing through the jejunostomy opening. Then the diet consisted of 750 cc. of milk and cream and two eggs given in three feedings daily through the opening. In addition, during the second week, only about 250 cc. of water was given by mouth daily. During the third week 5 Gm. of sodium chloride was given daily with the feedings. Vomiting occurred about three times a week. The animal passed two or three very soft stools daily. The weight gradually declined from 18 Kg. to 11.4 Kg. on the twenty-third day, when the dog died. Chemical examination of the blood showed a moderate rise in chlorides from 520 to 640 mg. per hundred cubic centimeters, and only slight fluctuation in the carbon dioxide and nonprotein nitrogen. (Figure 2 shows weight and readings made on chemical examination of the blood.) Autopsy showed no evidence of complication. The obstructed portion of the bowel was 67 cm. long and was not distended.

*Dog 88.*—During the first ten days following the obstruction and jejunostomy the feedings consisted of 250 cc. of milk and cream, one egg and 1 Gm. of sodium chloride given three times a day. During the following days the amount of milk and cream was cut down to 100 cc. given seven times a day. Occasionally an egg was added but no sodium chloride. The weight declined from 19 to 13.7 Kg. Vomiting occurred on at least eight days. About two soft stools were passed daily. The animal died on the twenty-first day without any apparent sign of terminal weakness. Chemical examination of the blood showed a slight rise in chlorides from 443 to 510 mg. per hundred cubic centimeters. The nonprotein nitrogen rose to the high figure of 115 mg. per hundred cubic centimeters on the day of death, and the carbon dioxide dropped from 61 mg. before operation to 24 mg. on the last day (figure 3 shows the weight and the results of the chemical examination).

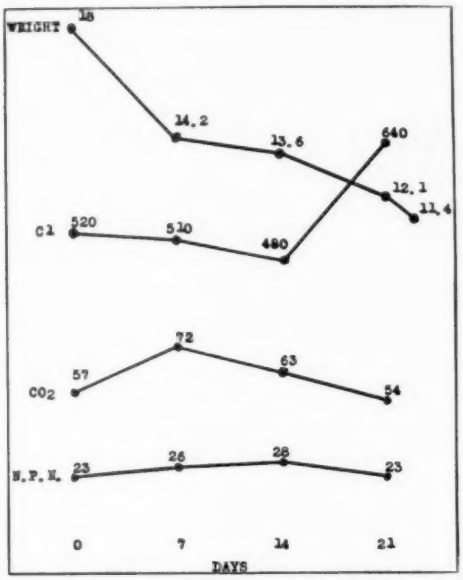


Fig. 2.—Weight and results of chemical examination of the blood of dog 96; death occurred on the twenty-third day.

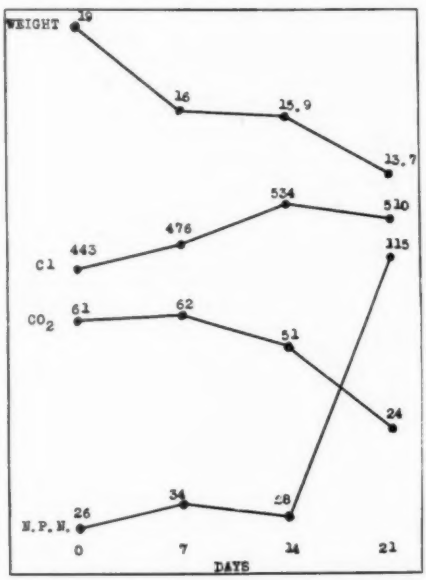


Fig. 3.—Weight and results of chemical examination of the blood of dog 88; death occurred on the twenty-first day.

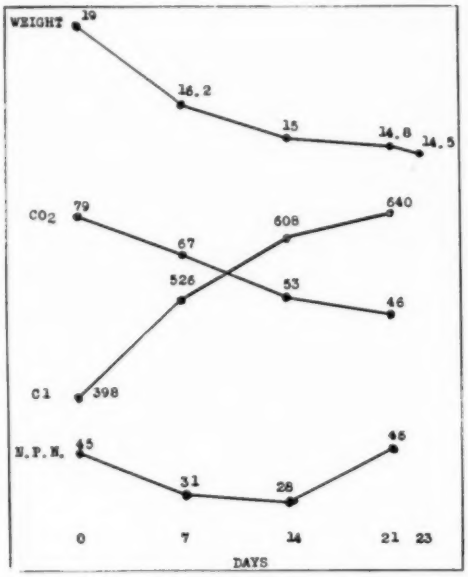


Fig. 4.—Weight and results of chemical examination of the blood of dog 945; death occurred on the twenty-third day.

Fig. 5.—Specimen from dog 945; the obstructed portion of the jejunum measured 65 cm.; death occurred on the twenty-third day.

Autopsy revealed marked bronchopneumonia. The obstructed portion of the bowel was 72 cm. long and showed no evidence of distention.

*Dog 945.*—The feedings were given three times a day for the first eleven days following the obstruction and jejunostomy as was done in the case of dog 88, and then seven times a day. The weight declined from 19 Kg. to 14.5 Kg. on the twenty-third day, when death occurred without any premonitory sign. The stools were practically of the same type as those reported for dog 88. Chemical examination of the blood up to the end of the third week showed a rise in chlorides from 398 mg. per hundred cubic centimeters before operation to 640 mg. two days before death. The carbon dioxide, which was originally somewhat higher than normal, dropped from 79 to 46 mg. The nonprotein nitrogen was originally 45 mg. and after a slight fall rose to 46 mg. (Figure 4 shows weight and results of chemical examination.) Autopsy showed only a small patch of bronchopneumonia. There was no evidence of a complication other than this. The obstructed portion of the bowel measured 65 cm. and was not distended. (Figure 5 shows the specimen.) The patch of pneumonia did not appear to be sufficiently extensive to explain completely the cause of death.

*Dog 919.*—During the first nine days following the obstruction and jejunostomy feedings were given three times a day and from then on seven times a day, as described for dog 88. No sodium chloride was given after the ninth day. The stools averaged two a day. Vomiting occurred at least ten times. The weight declined from 16 Kg. to 9.6 Kg. on the thirty-second day, when death occurred. During the last four days the animal became progressively weaker. Chemical examination of the blood up to the thirty-first day showed a very slight fall in chlorides from 492 to 460 mg. per hundred cubic centimeters, a rise in carbon dioxide from 52 to 71 mg. and a fall in nonprotein nitrogen from 33 to 27 mg. (Figure 6 shows weight and results of chemical examination.) At autopsy an extensive cervical cellulitis and mediastinitis were found, which were probably the result of the drawing of blood from the jugular vein. In addition there were an extensive bronchopneumonia and areas of necrosis and ulceration in the esophagus. The stomach was markedly dilated, but the obstructed portion of the jejunum was only slightly distended. (Figure 7 shows the specimen.) This portion of the jejunum measured 48 cm. in length. Gross blood was found in the stools the day before death, but no apparent source of the bleeding was found at necropsy.

*Dog 134.*—The feedings were 150 cc. of milk and cream given seven times a day for the first three weeks following the obstruction. Then 100 cc. was given ten times a day. About 15 cc. of pure gastric juice was added to each feeding from the eighteenth to the twenty-eighth day. The gastric juice was obtained from one of Dragstedt's [2] dogs which had a complete isolated pouch of the stomach. On the eighteenth day the gastric analysis of the obstructed animal showed a free acidity of 19 points and a total acidity of 81. On the thirty-fifth day there was no free acid present, but the combined acid was 68. The blood count on the twenty-eighth day was 70 per cent hemoglobin, 5,080,000 red blood cells and 7,000 white blood cells. On the thirty-fifth day the hemoglobin was also 70 per cent, but the red cells were 4,160,000 and the white cells were 8,400. Vomiting occurred about two or three times a week. Two or three stools were passed daily. These were soft and sometimes formed, but never watery. The weight slowly declined from 19.6 Kg. to 13.7 Kg. on the thirty-seventh day. Chemical examination of the blood showed relatively little change during the first five weeks, but on the day of death

2. Dragstedt, L. R., and Ellis, J. C.: The Fatal Effect of the Total Loss of Gastric Juice, Am. J. Physiol. **93**:407 (June) 1930.

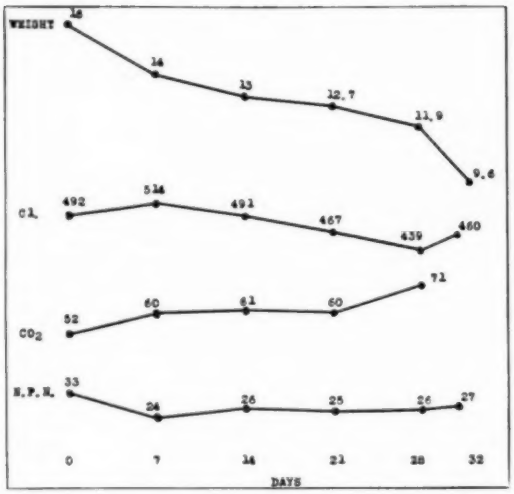


Fig. 6.—Weight and results of chemical examination of the blood of dog 919; death occurred on the thirty-second day.

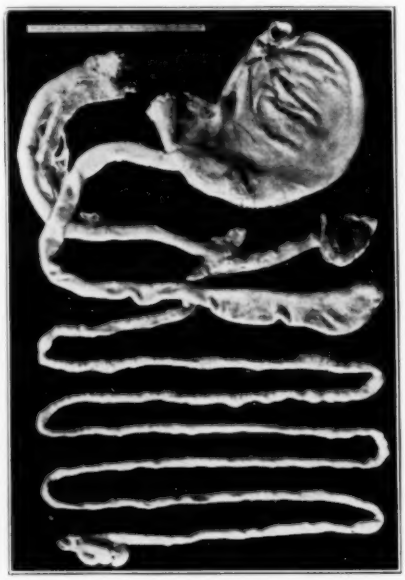

Fig. 7.—Specimen from dog 919, showing slight distention of the obstructed segment of jejunum, which measured 48 cm.; death occurred on the thirty-second day.

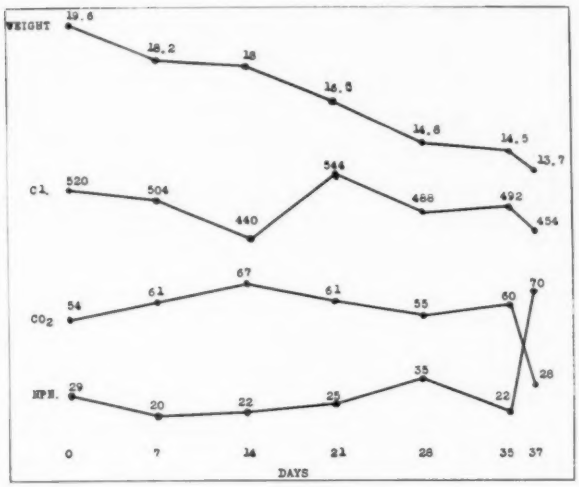


Fig. 8.—Weight and results of chemical examination of the blood of dog 134; death occurred on the thirty-seventh day.

Fig. 9.—Specimen from dog 134, showing slight distention of the obstructed segment of jejunum, which measured 80 cm.; death occurred on the thirty-seventh day.

the carbon dioxide dropped to 27 mg. per hundred cubic centimeters, and the non-protein nitrogen rose to 70 mg.; however, the chlorides were only slightly lower than the original figure of 520 mg., dropping to 454 mg. (Figure 8 shows the weight and chemical readings.) During the last two days the animal became progressively weaker until death occurred on the thirty-seventh day. Autopsy revealed no evidence of a complication. The obstructed portion of the bowel was 80 cm. long and was slightly distended, especially at the distal end (figure 9 shows the specimen).

## COMMENT

The cause of death in intestinal obstruction has been attributed by most clinicians and investigators to toxemia. The nature of this toxemia has not been definitely established. Recently some investigators[3] have drawn attention to a difference between simple high obstruction in which vomiting is a conspicuous feature and obstruction with damage to the blood supply of the bowel by distention or strangulation. They believe that death is due to toxemia in the latter, whereas in the former the lethal outcome is brought about by the loss of digestive secretions alone.

The interpretation of the results of this experiment is not altogether clear. The marked variability in length of life of the animals with intestinal obstruction, all treated in practically the same manner, can not be satisfactorily explained. However, there are several points that may be considered in comparing the two groups. In the first series, which survived only from four to twelve days, the animals were given large feedings two or three times a day, vomiting occurred frequently, especially after feeding, and diarrhea was often present. There was no distention of the obstructed portion of the bowel at autopsy, and chemical examination of the blood showed a slight rise in chlorides. In the second series, which lived from three to five weeks, the nursing was better, the feedings were given more frequently and in smaller amounts at least part of the time, the dogs were larger with one exception, vomiting occurred less frequently and seldom following or during a feeding, and diarrhea was not present.

In comparing this experiment with that described in the previous communication,[1] the only outstanding difference in the way the animals were treated was in the addition of food and sodium chloride below the obstruction. Although, from no apparent cause other than the obstruction, some of the animals died much sooner than those that received

3. Gatch, W. D.; Trussler, H. M., and Ayres, K. D.: Causes of Death in Acute Intestinal Obstruction, Surg., Gynec. & Obst. **46**:332 (March) 1928. McIver, M. A., and Gamble, J. L.: Body Fluid Changes Due to Upper Intestinal Obstruction, J. A. M. A. **91**:1589 (Nov. 24) 1928. White, J. C., and Fender, F. A.: The Cause of Death in Uncomplicated High Intestinal Obstruction, Arch. Surg. **20**:897 (June) 1930. Morton, J. J., and Pearse, H. E.: The Similarity in Effect of Experimental High Intestinal Obstruction and High Complete Intestinal Fistula, Ann. Surg. **94**:263 (Aug.) 1931.

no food, one animal was kept alive longer with the feedings than any of the animals in the previous experiment. The changes in the chemical constituents of the blood were rather marked in the series of animals referred to in the previous report; that is, there were a fall in chlorides and a rise in carbon dioxide and in nonprotein nitrogen. However, in this experiment there was not a single instance of a marked fall in chlorides. The most noticeable fall in chlorides was from 520 to 454 mg. per hundred cubic centimeters in dog 134, which lived thirty-seven days. In the animal that lived thirty-two days there was only a slight fall from 492 to 460 mg. In all the others there was a rise in chlorides. The nonprotein nitrogen was more inclined to show a rise than a fall, and the carbon dioxide showed more of a tendency to fall than to rise. However, the changes were seldom marked for either.

The fall that was observed in the blood chlorides in the previous experiment [1] could be accounted for on the basis of loss of gastric juice as observed in simple pyloric obstruction [4] or as shown by Dragstedt [2] in complete isolated pouches of the stomach. However, the presence of a short loop of jejunum offered opportunity for resorption of enough of the gastric juice to prevent the rapidly fatal outcome of complete loss of gastric juice that occurs in pyloric obstruction or in complete pouches of the stomach. In this experiment, in addition to the short loop of jejunum which permitted some resorption of gastric juice, there was opportunity below the obstruction for absorption of sodium chloride in the milk itself or added to the milk, and in one instance of gastric juice, which replaced the chlorides that had been lost in the vomitus. This would probably account for the maintenance of the blood chlorides at a fairly high level during the period of obstruction.

Milk contains approximately 0.13 per cent of sodium chloride.[5] In several animals there was a considerable period when sodium chloride was not added to the feedings, and the maintenance of the blood chlorides at a fairly high level during these periods was apparently due to the sodium chloride in the milk. In dog 134 no sodium chloride was added to the feedings. At the end of two weeks the blood chlorides had fallen only from 520 to 440 mg. per hundred cubic centimeters; the latter figure was considerably higher than that for the blood chlorides at the end of two weeks in any of the animals of the previous experiment. However, when the gastric juice was added to the feedings from the eighteenth to the twenty-eighth day, there was a moderate rise in blood chlorides during that period. In dog 919 sodium

4. Hastings, A. B.; Murray, C. D., and Murray, H. A.: Certain Chemical Changes in the Blood After Pyloric Obstruction in Dogs, J. Biol. Chem. **46**:223, 1921.

5. Van Slyke, L. L., and Bosworth, A. B.: Condition of Casein and Salts in Milk, J. Biol. Chem. **20**:135, 1915.

chloride was added only during the first nine days. From then on the sodium chloride in the milk was apparently adequate to keep the blood chlorides fairly high during the rest of the thirty-two days of obstruction. In dogs 88 and 945 sodium chloride was added only during the first half of the period of obstruction; however, the blood chlorides showed no tendency to fall.

The diet in this experiment was calculated to contain more calories than would be necessary for maintenance; however, all the animals lost weight. The animal that lived thirty-seven days lost 5.9 Kg. This was an average of 0.16 Kg. per day, as compared with the daily loss of 0.32 Kg. per day in the animal that lived thirty-three days in the previously reported experiment without feedings. This would tend to show that while starvation may influence the length of life in obstruction it was not the determining factor in the cause of death, at least in this experiment.

The results of an experiment similar to this one have been recently published by Pearse.[6] In addition to short-circuiting the biliary, pancreatic and duodenal secretions below the obstruction, the pyloric part of the stomach was also drained below the obstruction, while the fundus drained into the obstructed segment of jejunum. Gastrostomy was performed in the pyloric section of the stomach, and milk was administered, together with some sodium chloride. Some of the animals were kept alive a month in this manner; then they were killed. There was no more evidence of toxemia in these animals than was observed in the dogs described in this paper. The blood showed only a slight tendency to decrease in chlorides, and as soon as a fall occurred the administration of sodium chloride into the bowel would bring the chlorides back to a higher level.

## SUMMARY

1. When high intestinal obstruction was produced in dogs with the biliary, pancreatic and duodenal secretions short-circuited below the point of obstruction and the animals fed milk and cream, with sodium chloride sometimes added, through a jejunostomy opening below the obstruction, some animals lived from three to five weeks, while others did not survive longer than from four to twelve days. (Table 2 gives the length of life, the weight and the length of the obstructed portion of the bowel.)

2. The animals usually remained in fairly good condition until shortly before death.

6. Pearse, H. E.: Is Toxaemia the Cause of Death in Uncomplicated Intestinal Obstruction? Ann. Surg. **93**:915 (April) 1931.

3. Vomiting throughout the period of obstruction was a conspicuous feature in some animals, while in others it did not occur oftener than three times a week.

4. The weight showed a gradual decline in spite of the high caloric value of the food taken. The loss of weight was less marked when the feedings were frequent and small.

5. Chemical studies of the blood showed no marked fall in chlorides. In two instances there was a slight fall, but the amount of chlorides was still within the range of normal, while all the other animals showed a rise. The carbon dioxide and nonprotein nitrogen showed no marked constant changes.

6. In the first series of six animals which lived from four to twelve days, autopsy revealed in only one animal evidence of a complication

TABLE 2.—*Length of Life, Weight and Length of Obstructed Bowel*

| | Dog | Length of Life (Days) | Weight (Kg.) | Obstructed Bowel (Cm.) |
|---|---|---|---|---|
| Series I | 19 | 4 | 30.0 | 90 |
| | 83 | 5 | 11.2 | 23 |
| | 872 | 8 | 11.7 | 55 |
| | 86 | 7 | 13.0 | 25 |
| | 918 | 11 | 23.2 | 40 |
| | 942 | 12 | 13.0 | 35 |
| Series II | 96 | 23 | 18.0 | 67 |
| | 88 | 21 | 19.0 | 72 |
| | 945 | 23 | 19.0 | 65 |
| | 919 | 32 | 16.0 | 48 |
| | 134 | 37 | 19.6 | 80 |

that would explain death as due to any other factor than the presence of an obstruction. In the second series of five dogs which survived from three to five weeks, death was definitely due to a complication in two animals and possibly in three. There was no appreciable distention of the obstructed portion of the bowel except in the two animals that lived thirty-two and thirty-seven days.

## CONCLUSIONS

1. The variability of the length of life of the animals with high intestinal obstruction in these experiments cannot be easily explained by either the toxic theory or that of the loss of digestive secretions.

2. The prolonged life of the animals in the second series that lived from three to five weeks, however, does appear to fit in with the theory of loss of digestive secretions.[7] This increased length of life compared with that of animals with simple obstruction at approximately the same

7. Dragstedt, L. R.: Failure of Reabsorption of Gastric and Pancreatic Juice, Am. J. Surg. **11**:544 (March) 1931.

level may possibly be due to the resorption of the biliary, pancreatic and duodenal secretions below the point of obstruction, along with some resorption of gastric juice in the obstructed segment of jejunum. It also appears that the maintenance of the blood chlorides at a fairly high level during the period of obstruction as compared with the fall in chlorides observed in the previous experiment [1] was due to the replacement of chlorides lost in the vomited gastric juice by the sodium chloride present in the milk, as well as by that which was added to it, and in one instance by gastric juice.

3. Nevertheless this does not explain why the animals in the first series except in one instance died in from four to twelve days without a fall in chlorides, without distention of the obstructed bowel and without any other apparent cause than the presence of an obstruction. Furthermore, it would be difficult to explain the death of the animals in this series on the basis of toxemia when there was practically no distention of the obstructed portion of the bowel.

# WHITMAN RECONSTRUCTION OPERATION ON THE HIP JOINT

## AN ANALYSIS OF LATE RESULTS

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In 1921, Whitman [1] reported an operative procedure for ununited fracture of the neck of the femur which resulted in a stable, painless hip with satisfactory motion. This differed widely from bone pegging and the Brackett operations inasmuch as the femoral head was removed, the femoral neck placed into the acetabulum and the greater trochanter transplanted downward on the shaft. Four years later, Rechtman [2] reported thirty-four cases from Whitman's service in which this operation had been performed. He broadened the indications to cover not only nonunion of fracture of the neck of the femur but also to include malum coxae senilis, quiescent tuberculous hip, acute epiphysitis and Charcot hip. In 1926, Armitage Whitman [3] presented the late results in nine cases. His patients had an average motion of 45 degrees flexion and 10 degrees abduction. Four of these patients used a cane. All had diminished pain following the intervention. In the orthopedic department of the State University of Iowa, eighteen patients have had the Whitman reconstruction operation performed for ununited fracture of the neck of the femur and for arthritides of the hip. This report represents an analysis of the final results.

### INDICATIONS

The Whitman reconstruction operation was devised to correct the deformity and to produce a stable joint that allows motion without pain. We therefore believe that the operation is applicable primarily, of course, in ununited fracture of the neck of the femur and, secondarily, in a pathologic dislocation of the hip, in old slipped femoral epiphyses

From the Department of Orthopedic Surgery, State University of Iowa, Iowa City.

1. Whitman, Royal: The Reconstruction Operation for Ununited Fracture of the Neck of the Femur, Surg., Gynec. & Obst. **32**:6 (June) 1921.

2. Rechtman, A. M.: The Reconstruction Operation on the Hip, Arch. Surg. **11**:842 (Dec.) 1925.

3. Whitman, Armitage: Remarks Preparatory to a Cinematographic Presentation of Late Results of the Reconstruction Operation, J. Bone & Joint Surg. **8**:803 (Oct.) 1926.

and in osteo-arthritis or traumatic arthritis of the hip. In these conditions, pain, instability, loss of motion and deformity are the complaints. The Whitman reconstruction is suitable for meeting all of these symptoms.

### CONTRAINDICATIONS AND COMPLICATIONS

Because of the attending dangers and the possibility of complications, the operation cannot be carried out in all cases which present the foregoing symptoms. It is indicated only in good surgical risks. Age is an important factor. In the series of eighteen cases from the orthopedic department the average age was 46, the oldest patient being 63 and the youngest 16.

The operation is contraindicated in tuberculosis and arthropathy. Rechtman [2] reported the cases of two patients with quiescent tuberculous hips who developed sinuses following the operations. In our one case with Charcot hip in which the Whitman reconstruction method was used, there was postoperative acetabular destruction resulting in complete failure.

Of complications, embolism is prominently mentioned in the literature. Among seventy-four cases reported, three patients died of emboli, two had emboli but recovered and one died of shock. Other operative complications are shock and bronchopneumonia. The immediate postoperative complications encountered in our series, in spite of careful selection of cases and rigid adherence to restrictions in indications, are as follows:

| | |
|---|---|
| Uneventful | 7 |
| Slight shock | 2 |
| Moderate shock | 3 |
| Severe shock | 2 |
| Bronchopneumonia | 1 |
| Death | 1 |
| No data available | 2 |

### PROCEDURE

The Whitman reconstruction operation is based on three principal steps: first, the removal of the head; second, the insertion of the remaining neck or of the end of the shaft of the femur into the vacated acetabulum, and third, the transplantation of the greater trochanter with its muscular attachments downward on the shaft spine of the ilium of the femur.

The joint is approached by a J-shaped incision running longitudinally downward from the anterior superior spine of the ilium to below the base of the greater trochanter, and then backward, crossing the trochanteric region. The greater trochanter is chiseled off at its base along a line parallel to the long axis of the femoral neck. Its muscular attachments are left intact as it is retracted upwardly and laterally. After opening the capsule, the head is removed and the end of the neck smoothed off. The neck is then inserted deep into the acetabulum, with the shaft of the femur in 150 degrees abduction. While the extremity is held so, a bed

is prepared on the outer side of the shaft to receive the greater trochanter. The trochanter is then pulled down to its new bed and fastened by means of nails or heavy drillhole sutures.

A double hip spica is applied in abduction, extension and neutral rotatory position. The patient remains in bed in this cast for approximately from four to six weeks. He then is allowed up on crutches, still wearing a cast. Physical therapy is instituted from six to ten weeks after operation, according to the degree of fusion of the trochanter to the shaft, as seen in the x-ray picture.

## ANALYSIS OF FINAL RESULTS

*Length of Observation.*—Since 1926, when the first operation was performed in this clinic, eighteen patients have had a Whitman reconstruction operation. Of these eighteen, three patients could not be traced; the remaining fifteen have been checked up personally, except a few whose condition was ascertained by questionnaire. Dr. Steindler

Fig. 1.—Whitman reconstruction for ununited fracture of the neck of the femur. Two nails fastened the trochanter to the shaft. The patient had a good result.

operated on thirteen of these patients, and older members of his staff on the others, all using the foregoing technic. The average length of personal observation following operation has been twenty months, the longest four years and the shortest two months. Patients continue to improve and develop more motion for a year and a half; after this their condition remains practically stationary. No signs of arthritis developed in any of the cases.

*Shortening.*—In his first paper, Whitman remarked that occasionally the operation diminishes the preexisting shortening. One of our patients gained ¼ inch (0.63 cm.) in length as a result of the operation. On the other hand, another patient lost 3¾ inches (9.5 cm.) after the operation. The average change in length that could be attributed to the operation was 1 inch (2.5 cm.) shortening. However, mobility, favorable position and stability render this loss comparatively insignificant.

*Mobility.*—This operation was designed primarily to correct a deformity and produce a stable, painless hip. Whitman believed, at first, that motion was a secondary consideration. Since the operation is in reality an arthroplasty, we consider mobility an essential attribute of a good result. Commonly a flexion contracture occurs, but this is usually slight enough to be of no importance. This flexion contracture amounted in fourteen patients to an average of 14 degrees. The average free range of flexion was 67 degrees. Contractures did not occur

Fig. 2.—The arrow points to a compression fracture of the femoral head. After operation the patient was free from pain; the hip was movable and stable, and good result was obtained.

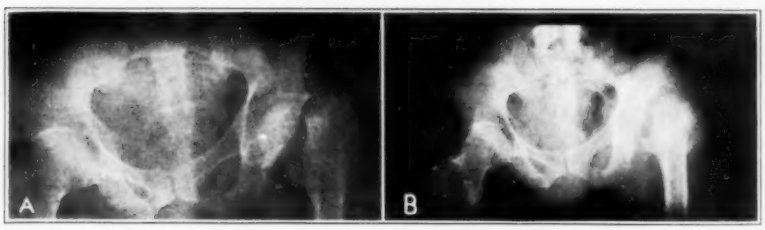


Fig. 3.—Charcot hip. *A*, before operation this was apparently an ordinary ununited fracture of the neck of the femur. *B*, after operation, the acetabulum disintegrated and the femur dislocated. Failure resulted.

in other than the sagittal plane of motion. Approximately 20 degrees adduction and 20 degrees abduction could be obtained. Internal rotation was usually limited. Such a degree of mobility in previously stiff or unstable joints was certainly satisfactory.

*Stability.*—One of the chief advantages of the reconstruction operation is a stable hip. With a smoothly rounded neck or end of the femoral shaft placed well in the acetabulum, as verified by postoperative x-ray pictures, stability is assured. From examination of fifteen

patients, fourteen were found to have a stable, weight-bearing joint (see table). Two of these fourteen even had a negative Trendelenburg sign. Eight of the fourteen needed no external support whatever. Four of these fourteen used some support for reasons other than inability to bear weight on the hip, e. g., two because of general osteo-arthritis, and one because of a posttyphoid transverse myelitis; one wore artificial limbs, both his legs having been amputated. The fifteenth patient had a Charcot hip. His acetabulum disintegrated; the joint telescoped and became unstable.

*Painlessness.*—Pain was the prime reason that caused the patients with ununited fracture of the neck of the femur or arthritis of the hip to seek aid by operation. The relief from pain is the main contribution of the reconstruction operation in these cases. All of the fourteen

*Late Postoperative Findings*

| | |
|---|---|
| 1. Pain | |
| None | 12 |
| Slight discomfort | 2 |
| No data available | 4 |
| 2. Stability | |
| Excellent (negative Trendelenburg sign) | 2 |
| Good (no support but positive Trendelenburg) | 8 |
| Stable (using support for extrinsic reasons) | 4 |
| Poor (telescoping) | 1 |
| No data available | 3 |
| 3. Average range of motion | |
| Flexion 166-99 degrees = 67 degrees | |
| Abduction 180-158 degrees = 22 degrees | |
| Adduction 180-161 degrees = 19 degrees | |
| Internal rotation = 8 degrees | |
| External rotation = 26 degrees | |

patients on whom data were secured in regard to this point were improved. Twelve patients had painless hips (see table). One patient had some discomfort. He had had a traumatic fracture dislocation, and the head was very difficult to remove. Roentgenograms showed that a small portion of the head had been left behind. Another patient had some discomfort for unknown reasons, but two observers who examined this patient separately noted that she had improved greatly.

## END-RESULTS

Only when pain, shortening, stability and mobility are considered together, may the final result of the Whitman reconstruction operation be ascertained. Among the fifteen patients on whom we have these late findings, eight had had an ununited fracture of the neck of the femur; two, osteo-arthritis of the hip; two, suppurative arthritis; one, generalized atrophic arthritis; one, traumatic dislocated hip and one, Charcot hip. Of these fifteen patients, eleven had good results. The

result was good in all (eight) cases of ununited fracture of the neck of the femur. The end results in the eighteen cases are as follows:

| | |
|---|---|
| Good | 11 |
| Fair | 3 |
| Failure | 1 |
| No late findings | 3 |

## ANALYSIS OF POORER RESULTS

The good results need no further discussion. However, further consideration should be given to the other four cases. Among them is a patient with a destructive arthritis of the hip. The femoral head, in her case, had to be chiseled from the acetabulum. After one and a half years of observation she has a painless, stable but ankylosed hip. She walks with only a slight limp. Because of the lack of motion this case is classified as a fair result. Another patient had bilateral suppurative arthritis of both hips with bony fusion of one and a partially destroyed and unstable joint on the other. A reconstruction was done on the latter with very little benefit. Although the patient has a painless hip with a negative Trendelenburg sign, yet the ranges of motion of the hip on which the operation was performed are so limited that, with the other joint fused, he has to use crutches when walking any moderate distance. Whether an arthroplasty of the opposite hip would provide a better result for the reconstruction is a matter of conjecture. This result as it now appears is only fair. A third patient had generalized arthritis with a partially ankylosed and painful hip. After the first operation the greater trochanter failed to fuse with the shaft, and the neck of the femur dislocated, so that a year later another operation was performed. Now, four years after the last operation, she has a painless, stable, movable joint, but there is a shortening of 4 inches (10.16 cm.). Because of the great inequality of length of the extremities, this is considered only a fair result. Another patient had an ununited fracture of the neck of the femur. He had a positive Wassermann reaction, and was given antisyphilitic therapy before operation. Immediately following the operation the acetabulum rapidly disintegrated, and loose bony masses formed about the hip. Definite tabetic symptoms became evident for the first time. The diagnosis was changed to Charcot hip. With the loss of the acetabular roof, the femur dislocated, giving the patient a useless hip. This case is the only complete failure in this series.

## SUMMARY

An analysis of the end-results of fifteen cases in which a Whitman reconstruction operation was performed has been made. This operation is indicated in ununited fracture of the neck of the femur and arthri-

tides of the hip to alleviate pain, deformity, instability and to allow useful ranges of motion. The operation carries a moderate surgical risk. All patients who were operated on because of ununited fracture of the neck of the femur showed a good result. The final outcome is less certain in patients with arthritic lesions; yet the results obtained were satisfactory enough to make the operation advisable also in this group of cases.

# CHANGES IN THE SYMPHYSIS PUBIS AND SACRO-ILIAC ARTICULATIONS AS A RESULT OF PREGNANCY AND CHILDBIRTH

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For a certain length of time the idea existed that during labor the entire pelvic ring is incapable of any change in size. Clinical observations, however, support the assumption that during pregnancy and labor not only is a certain amount of movement possible in the pelvic joints, but a distinct stretching or widening takes place. Some of these observations are directly confirmable; others can be made during actual labor.

The normal articular cavities of the symphysis pubis and the sacro-iliac joints are the anatomic basis for the movements of the pelvic joints in pregnancy and labor. During pregnancy a relaxation of the strong ligaments in the sacro-iliac joints and the symphysis pubis occurs and makes possible an increased mobility. The importance of this increased mobility lies in the possibility of a change in size of the pelvic ring. This relaxation also prevents, to a certain degree, the forcible rupture of the ligaments, which under physiologic conditions are only slightly extensible.

The mobility of the pelvic joints and especially of the symphysis pubis in pregnancy was well known to Hippocrates, who spoke of the separation of the ossa pubis during labor. Morgagni, Spiegel and Harvey held the same opinion. Barkow[1] (1841), Luschka[2] (1864), Balandin (1871) and others likewise recognized this fact. Martius[3] (1930) and Müller[4] were able to give proof of the widening of the

From the Pathological-Anatomical Institute of the University of Innsbruck.

1. Barkow, quoted by Luschka, H.: Die Kreuzdarmbeinfuge und die Schambeinfuge des Menschen, Virchows Arch. f. path. Anat. **7**:299, 1854; quoted by Klein, G.: Zur Mechanik des Ileosarcralgelenkes, Ztschr. f. Geburtsh. u. Gynäk. **21**:74, 1891; footnote 2.

2. Luschka, H.: Die Anatomie des Menschen: Die Anatomie des menschlichen Beckens, Tübingen, H. Laupp, 1864, vol. 2, p. 88.

3. Martius, H.: Umbauformen und andere Anomalien der unteren Wirbelsäule und ihre pathogenetische Bedeutung, Arch. f. Gynäk. **139**:581, 1930.

4. Müller, W.: Röntgenologische Untersuchungen über die Symphyse Schwangerer, Zentralbl. f. Gynäk. **55**:999, 1931.

symphysis pubis by roentgen studies made immediately after labor, and by additional roentgenograms made six weeks post partum they demonstrated the reduction in the width of this point.

Different opinions exist regarding the manner of relaxation of the joints. According to R. Fick [5] the relaxation of the joints of the pelvic ring is due to a shifting of the center of gravity of a pregnant woman, and through this shifting, the posture is changed. Furthermore, during pregnancy the mobility of the symphysis is augmented in walking. This theory of Fick is corroborated by a comparative study of the symphysis pubis of men. Likewise, a greater mobility of the pelvis in its anterior part necessitates an increased gaping of the sacro-

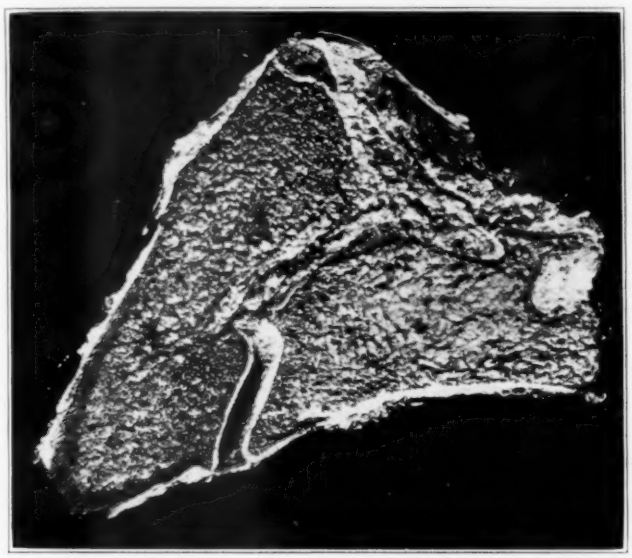

Fig. 1.—Gross specimen of a gaping articulatio sacro-iliaca during the second pregnancy of a 20 year old woman.

iliac joints. Thus the anterior ligaments of the sacro-iliac joints and the ligaments of the symphysis pubis are stretched, while the posterior sacro-iliac ligaments are relaxed. This increased mobility is utilized during labor and, if insufficient, may be augmented by the operative procedure of pubiotomy. Following such an operation the anterior sacro-iliac ligaments prevent widening beyond a certain point.

The mobility of the pelvis in pregnancy has been proved by roentgen studies made during this period. Von Schubert [6] demonstrated, by

5. Fick, R.: Bemerkungen über die Höhlenbildung im Schamfugenknorpel, Anat. Anz. **19**:307, 1901.

6. von Schubert, E.: Röntgenuntersuchungen des knöchernen Beckens im Profilbild: Exakte Messung der Beckenneigung beim Lebenden, Zentralbl. f. Gynäk. **53**:1064, 1929.

Fig. 2.—Microscopic section of the gross specimen shown in figure 1. There is considerable gaping of the joint.

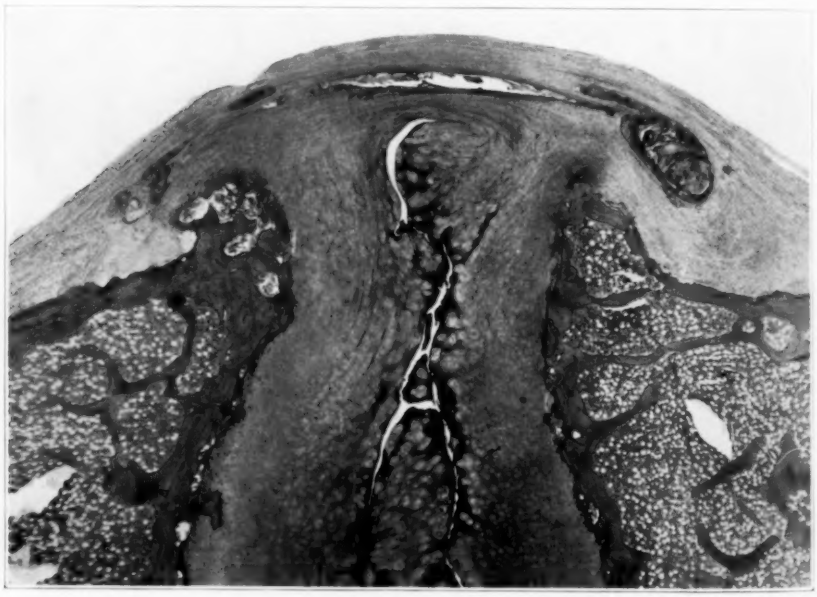

Fig. 3.—Symphysis pubis of a 48 year old woman, who had had two children. Cyst formation is visible near the terminal portions of the symphysis pubis (frontal section).

his researches on women at full term in the erect and prone positions, that the angle between the conjugata anatomica and the sacrum was from 5 to 8 degrees greater when the patient was standing. With the patient lying down, the conjugata vera was lengthened from 5 to 7 mm. Thus, clinical as well as anatomic observations show a possibility of widening of the pelvis during pregnancy and labor. This possibility of the considerable widening of the pelvic joints was clearly demonstrated by our own researches, consisting of roentgenograms, horizontal

Fig. 4.—Part of the ossification zone of the symphysis pubis of a 15 year old girl with depression of the ossification line due to degeneration of the ground substance of the cartilage.

sections and histologic study of cross-sections and of the joints. At the end of pregnancy and shortly after labor the joints were gaping (figs. 1 and 2).

The correctness of the findings of Fick concerning the mobility of the pelvic joints was substantiated by histologic studies. Enlargement of the cavity of the symphysis pubis as a result of increased activity has been found in men following heavy work. Thus it follows that this increased mobility is chiefly caused by mechanical strains and changes of posture.

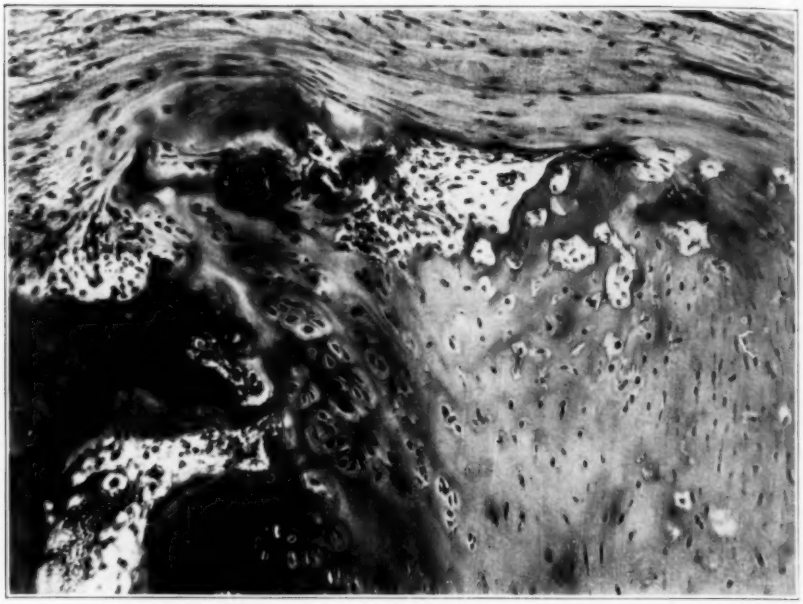

Fig. 5.—Microscopic fracture in the terminal parts of the symphysis pubis of an 11 year old girl.

Fig. 6.—Part of an articulatio sacro-iliaca of a 36 year old woman who had had seven children. Fissure formation in the joint cartilage is seen.

A further proof of increased mobility of the sacro-iliac joints and symphysis pubis is given by the frequent finding of cysts. These cysts are situated near the terminal portions of the joints (fig. 3); the lining is often partly synovial. About the symphysis pubis they are often situated beneath the soft tissues and the periosteum. Many of them are directly connected with the joint space. Within the cysts are small rounded fragments of cartilage and bits of tissue of varying size which have come from within the joints, the result of the rubbing together of the joint surfaces. The fragments often accumulate in the outer angles of the cysts and frequently lie in striae within the cysts,

Fig. 7.—Articulatio sacro-iliaca of a 27 year old woman who had had two children. Note the formation of marginal exostoses at the terminal parts of this joint. Hemorrhage has occurred in the joint cavity.

indicating that they have been given off by the joint at different intervals. The formation of these cysts and the character of their lining and contents indicate a certain necessity for mobility of these joints. Of further importance is the fact that none of the sacro-iliac joints and scarcely any symphysis pubis investigated were free from pathologic changes. A distinction must be made between the changes due to trauma and those due to osteoarthritis deformans, as well as to secondary diseases of the joints. In children and young persons up to the time of the completion of ossification, small areas of liquefaction and mucoid degeneration of the ground substance of the cartilage

occur. Ossification does not progress in these foci, and the result is an indentation or depression in the zone of ossification (fig. 4). These effects of mechanical trauma are especially well seen in the terminal parts of the joints; they are characterized by numerous minute areas of damage, microscopic fractures, fissure and cyst formation and hemorrhages (fig. 5). The result of such injuries is the separation and rounding off of fragments and callus formation. Pregnancy affords

Fig. 8.—Fissure formations in the cartilage of the symphysis pubis of a 36 year old woman who had had seven children.

the opportunity for the occurrence of slight traumas with sequelae similar to those first described in studies of arthritis deformans of the hip joint (Lang[7]). Because of the greater hyperemia and increased vulnerability of the pelvic tissues during pregnancy, functional activity is more irritating and increasingly so toward the end of pregnancy. If

7. Lang, F. J.: Mikroskopische Befunde bei juveniler Arthritis deformans, Virchows Arch. f. path. Anat. **239**:76, 1922; Zur Kenntnis der Veränderungen der Hüpfanne bei Arthritis deformans, ibid. **252**:578, 1924.

changes remain from previous pregnancies or if changes of a static or mechanical nature, as for example a lordosis, are present, such changes can be accentuated during subsequent pregnancies and labors.

Functional or traumatic changes, especially in the cartilage of the pelvic joints, are of great importance for the origin of reactive and proliferative processes of arthritis deformans in these joints. Apart from the lacerations and fissure formations resulting from successive pregnancies and labors, the sequelae of traumatic changes remaining from childhood are especially noteworthy for the production of arthritis deformans. All the characteristics of arthritis deformans can be

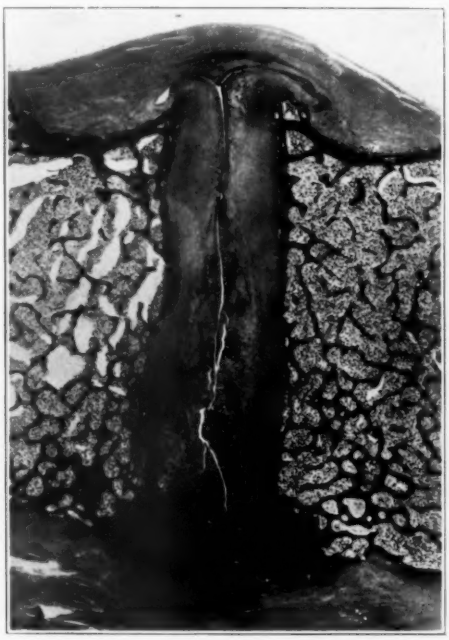

Fig. 9.—Symphysis pubis of a 52 year old woman who had had three children. The formation of a T-shaped cleft is seen (see fig. 10).

observed, namely, changes in the cartilage with loss of its normal elasticity (fig. 6), vascularization and ossification invading the cartilage from the subchondral zone, extreme erosion of the surface with polishing and the formation of marginal exostoses (fig. 7). The so-called growth processes in the pelvis bones during pregnancy can be traced to reactive processes that arise from damage to the cartilage. These injuries to the cartilage are accompanied by vascularization and formation of bone in the deeper parts of the cartilage.

Changes that must be considered as a permanent dilatation of the pelvis are found in the extensive fissure formations and T-shaped

clefts of the symphysis pubis (figs. 8 to 10). These can be seen at the end of pregnancy and in women who have given birth to full term infants. In like manner, the occasionally observed true joint of the symphysis pubis is the result of an adaptation to functional activity.

Marked differences can be shown in the symphyses pubis of women at the end of pregnancy and shortly after delivery, as contrasted with those of women who have had a delivery several years previously. In the symphysis pubis of a woman at the end of pregnancy and shortly after labor, extensive splitting of the cartilage lining the joint is found. Such splitting is not present in the cartilage of the symphysis pubis of

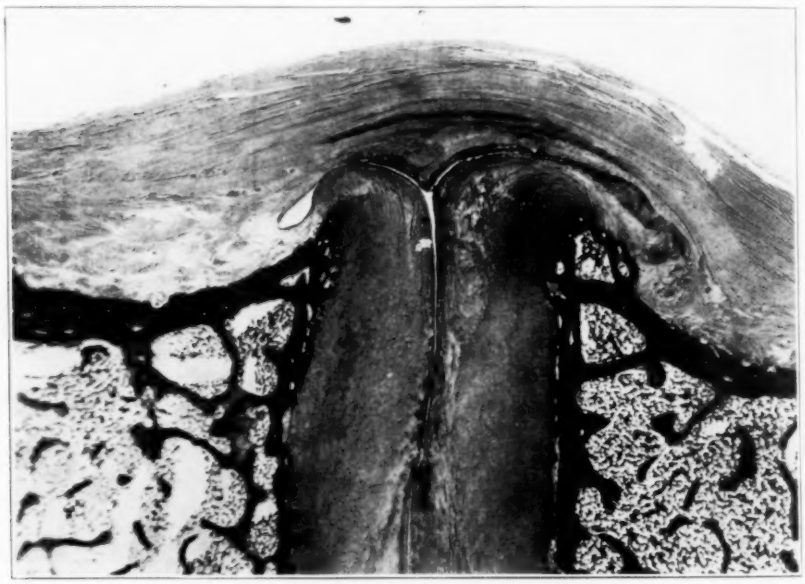

Fig. 10.—Part of area shown in figure 9, with the T-shaped cleft in the inner part of the symphysis.

a woman who has had a delivery years before. Instead the surfaces of the cartilage are smooth and approximated. It appears that the split cartilage becomes entirely separated and is forced out into the cysts; the fragments of cartilage and tissue clearly prove this.

The finding of recent and old hemorrhages in the cavities of the sacro-iliac joints must be mentioned. The hemorrhages are the result of trauma to these joints. Larger hemorrhages are found as the sequel to the disproportion between normal extensibility of the joint and that due to necessity (fig. 5). They follow trauma during labor, and furthermore can arise from the increased stress on the ligaments occurring at the end of pregnancy. The hyperemia of the ligaments and the

synovial tissues during pregnancy explains the extravasations of blood as congestive hemorrhages.

The investigations discussed prove that changes in the sacro-iliac joints must be considered as a cause of the backache that is so frequent in pregnant women and in those who have had many labors. This fact has recently received increased attention from gynecologists and orthopedic surgeons following the demonstration that backache can result from anatomic changes of the vertebrae and their connections with the sacro-iliac joints.

## CONCLUSIONS

These studies place on an anatomic and histologic basis the clinically recognized gaping of the pelvis in pregnancy and labor. They show the development of this widening and the alterations that the pelvic joints thereby suffer. They present the late sequelae leading directly or indirectly to permanent changes in the joints. Finally, they indicate that pregnancy and labor, with their disturbances of the static mechanical relationships of the pelvis, are not inconsequential factors in the etiology of arthritis deformans.

# SYPHILIS OF THE STOMACH

## REVIEW OF THE LITERATURE AND REPORT OF A CASE

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Although the clinical diagnosis of syphilis of the stomach is made frequently and such cases are reported in large numbers, histologically proved instances of the disease are rare. A case seen recently at the University of Virginia Hospital seems to present sufficient histologic evidence of syphilis of the stomach to warrant a report and a brief review of the stricter criteria demanded for the diagnosis.

An idea of the apparent rarity of proved instances of the disease may be gained from Hartwell.[1] In 1925, he reviewed more than 200 cases that had been recorded previously in the literature as syphilis of the stomach, and he concluded that in all but 27 of these the evidence presented was insufficient to prove the diagnosis. Hartwell's review of the subject was comprehensive and scientifically critical. He stated that Andral [2] had reported 2 cases of supposed syphilis of the stomach as early as 1834. To Chiari,[3] however, he attributed the first significant contribution to the subject. Chiari had emphasized the rarity of histologically proved cases and had found only 7 previously reported cases that conformed to the strict criteria that he promulgated.

Following the introduction of the Wassermann reaction (1906) and gastro-intestinal roentgenology (1909-1912), however, numbers of cases were reported, the diagnosis based, all too frequently, on purely presumptive or insufficient and unsound clinical evidence. Many reports contain no more convincing evidence than the combination of an upper abdominal complaint, roentgenologic evidence of gastric disease and a positive Wassermann reaction. Graham [4] reported the first histologically proved case in which the tissues had been removed surgically.

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1. Hartwell, J. A.: Syphilis of the Stomach: A Critical Review of Reported Cases from the Pathological and Clinical Viewpoints, Ann. Surg. **81**:767, 1925.

2. Andral, Gabriel: Cliniques, Paris **2**:201, 1834; quoted by Hartwell (footnote 1).

3. Chiari, H.: Ueber Magensyphilis, Internat. Beitr. z. wissensch. Med. Festschr. R. Virchow **2**:295, 1891.

4. Graham, E. A.: Surgical Treatment of Syphilis of the Stomach, Ann. Surg. **76**:449, 1922.

Necropsy statistics reveal a low incidence of the disease, even among syphilitic patients. Symmers,[5] in a series of 4,880 necropsies, found 314 syphilitic patients, but among these only 1 case of gastric syphilis. Singer and Meyer[6] stated that in 5,000 necropsies, with almost 10 per cent syphilitic patients, no case of gastric syphilis had been found. During the same six year period, however, 4 cases of histologically proved gastric syphilis had been discovered at operation. They attributed the greater surgical incidence of the disease to the increase in the frequency of resection of the stomach in recent years. Furthermore, these data led them to believe that retrogression or healing of gastric syphilis may occur. Study of their resected specimens substantiated this hypothesis. In the same stomach they differentiated various phases of syphilis, from changes characteristic of the height of the tertiary stage to those of dense fibrous overgrowth with widely scattered accumulations of round cells the syphilitic origin of which it was difficult to prove.

The type of case that has been responsible for the greatest confusion in the literature is that in which the history, the roentgenologic and laboratory findings, the resistance to all forms of treatment except specific and the prompt response to antisyphilitic treatment have made the diagnosis of syphilis of the stomach seem probable and reasonable. No doubt syphilis of the stomach has actually existed in some of these instances. In many of them, however, a subsequent necropsy has failed to disclose histologic proof.

For this reason all pathologists and many clinicians now insist on histologic proof of the diagnosis. In this connection it is interesting to note that spirochaeta pallida has been found in only 1 of the reported cases. McNee[7] found the organisms in the wall of the stomach, but only after prolonged search through many sections taken from various portions of the stomach and stained by the Levaditi technic.

## CLINICAL FEATURES

Hartwell, after a careful study of the literature, felt that "there are no characteristic subjective symptoms or objective findings upon which a diagnosis of syphilis of the stomach may soundly rest." He stated 5 clinical features that, when found in combination, had been considered more or less diagnostic: (1) positive Wassermann reaction; (2) a gastric anacidity or markedly reduced hydrochloric acid content;

5. Symmers, Douglas: Anatomic Lesions in Late Acquired Syphilis: A Study of 314 Cases Based on the Analysis of 4,880 Necropsies at Bellevue Hospital, J. A. M. A. **66**:1457 (May 6) 1916.

6. Singer, H. A., and Meyer, K. A.: Syphilis of the Stomach, with Special Reference to Its Incidence, Surg., Gynec. & Obst. **48**:23, 1929.

7. McNee, J. W.: Syphilis of the Stomach, Quart. J. Med. **15**:215, 1921-1922.

(3) marked deformity of the stomach roentgenologically, particularly of the "dumb-bell" type, or with an abrupt margin between the healthy and diseased portions of the stomach; (4) less marked cachexia, emaciation and anemia than would be found with such radiographic changes due to lesions other than those of syphilis; (5) improvement under antisyphilitic treatment. Each of these, however, was shown to be inconstant and undependable.

### RADIOLOGICAL CHANGES

Carman [8] mentioned 8 suggestive radiologic changes:

(1). Filling defect of the gastric outline, usually without corresponding palpable mass. (2). Shrinkage of gastric capacity. (3). Stiffening and lessened pliability of the gastric wall. (4). Absence of peristalsis from the involved area. (5). Pylorus gaping rather than obstructed. (6). Six-hour retention less common than in other gastric lesions (23 per cent). (7). So-called hour glass stomach; upper loculus expanded and bulbous, lower one tubular, due to extensive, irregular, concentric contraction. (8). Patient usually under cancer age and not ill in proportion to the extent of disease shown by the X-ray.

He felt, however, that these suggestive radiologic signs were much more uncertain even than the clinical signs.

### HISTOLOGIC CRITERIA

Accurate pathologic descriptions have been given by Chiari,[3] Flexner,[9] Stolper,[10] Pappenheimer and Woodruff,[11] McNee [7] and Brams and Meyer.[12] The disease apparently is initiated by the formation of a gumma in the submucosa and extends from there into the other coats. Through the breaking down of the gumma, particularly because of the action of the gastric juice, ulcers and ultimately scars may form; then only by the finding of other gummas or the remains of gummatous tissue can the syphilitic nature be established.

Grossly, the involved portion of the stomach is usually markedly thickened, most of the proliferation being present in the submucosal

8. Carman, R. D.: Syphilis of the Stomach in Its Roentgenologic Aspects, Am. J. Syph. **1**:111, 1917; Roentgenologic Aspects of Hour-Glass Stomach, Surg., Gynec. & Obst. **27**:426, 1918.

9. Flexner, S.: Gastric Syphilis, with a Report of a Case of Perforating Syphilitic Ulcer of the Stomach, Am. J. M. Sc. **116**:424, 1898.

10. Stolper, P.: Beiträge zur Syphilis visceralis, Magen-, Lungen- und Herzsyphilis, Cassel, T. G. Fisher & Company, 1896, pp. 43; quoted by Hartwell (footnote 1).

11. Pappenheimer, A. M., and Woodruff, I. O.: A Case of Syphilis of the Stomach, M. & S. Rep. Bellevue Hosp. **2**:219, 1905-1906; quoted by Hartwell (footnote 1).

12. Brams, W. A., and Meyer, K. A.: Gastric Syphilis: A Report of Two Cases Proved Anatomically, Surg., Gynec. & Obst. **37**:127, 1923.

layer. Ulceration is usually found, but it may differ in no distinctive way from that of a simple gastric ulcer. Suggestive features are a tendency to be quite large, an irregular serpiginous border, a firm smooth base and a demonstrable thickening of the wall of the stomach at a considerable distance from the ulcer itself. Unbroken gummas may be found occasionally.

Microscopically, gummas are of course most surely diagnostic. Other changes consist of endarteritis, endophlebitis, obliterating endarteritis and infiltration, especially the perivascular "signet-ring" type, with lymphocytes, plasma cells and eosinophilic leukocytes. Occasional giant cells may be found. Turnbull [13] sounded a note of warning against mistaking the similar pathologic changes following chronic inflammations due to pyogenic organisms with the changes due to syphilis.

## REPORT OF CASE

*History.*—H. E. F., a white man, aged 48, unmarried, was admitted to the University of Virginia Hospital on Nov. 25, 1929, complaining of "stomach trouble" of eight months' duration. In March, 1928, he had begun to suffer with a gnawing sort of pain in the upper part of the abdomen, especially on the left side. The pain had been most severe shortly after the ingestion of a meal, particularly the midday meal. Drinking milk or taking soda had given partial, temporary relief. Vomiting had occurred frequently, and he had lost 40 pounds (18 Kg.). There had been no hematemesis, melena, jaundice or clay-colored stools.

He had first consulted a physician in May, 1929, and had been told that he had "gastritis." He had consulted two other physicians without relief, and finally in September, 1929, a fourth physician had advised a roentgenologic examination of the stomach. This examination had revealed a "growth in the stomach" that had been taken to be malignant. The patient was referred to me for surgical treatment.

The patient's past history was irrelevant except for two attacks of gonorrhea several years previously and a chancre on the penis three years prior to the time of admission. There had been no cutaneous rash and no antisyphilitic treatment except for an ointment applied to the primary lesion. The chancre had healed in about ten days.

*Examination.*—Examination revealed a rather emaciated white man with dry skin and some loss of strength. His temperature was normal. The systolic blood pressure was 135, the diastolic 80. The mucous membranes were not pale; the sclerae were not bile tinged. The pupils were regular, and equal in size, but reacted somewhat sluggishly to light and in accommodation. The teeth were carious, and there was some pyorrhea alveolaris. There was no glandular enlargement. The heart and lungs were apparently normal. The abdomen was scaphoid. The edge of the liver was palpable. There was a movable, slightly tender mass about 5 cm. in diameter situated in the epigastrium just to the left of the midline. Both inguinal rings were very large, and there was some herniation. The patellar and other reflexes were normal.

13. Turnbull, in discussion on Monod, G.: Syphilis of the Stomach, Proc. Roy. Soc. Med. **15**:1, 1921-1922; quoted by Hartwell (footnote 1).

Urinalysis revealed no abnormality. The hemoglobin was 80 per cent (Dare); the red corpuscles numbered 4,360,000, the leukocytes 4,400, and the smear did not show any abnormality. The Wassermann reaction of the blood was strongly positive on several occasions. The stool contained no blood. Gastric analysis demonstrated marked retention without evidence of free hydrochloric acid. Lactic acid, occult blood and Oppler-Boas bacilli were present in the material. The Wassermann reaction of the spinal fluid was strongly positive. A roentgenologic examination of the chest gave negative results; the results of an examination of the stomach, made on Nov. 27, 1929, were reported as follows: "The esophagus

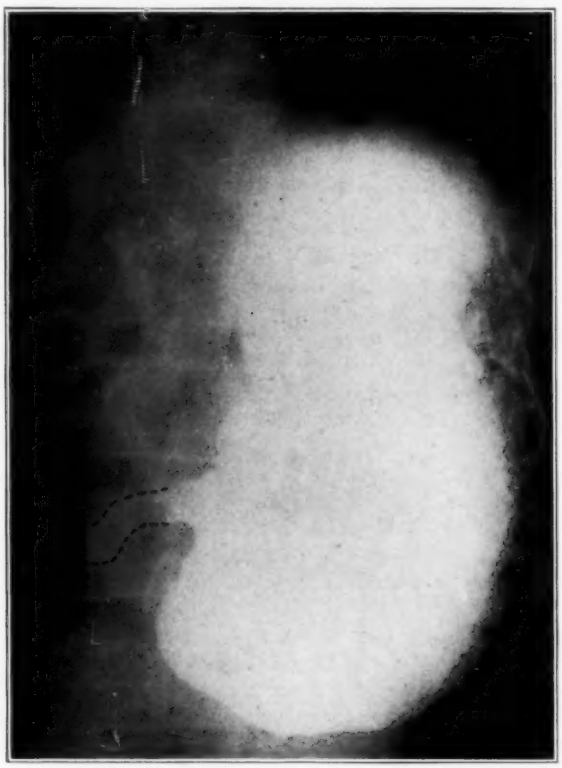

Fig. 1.—Roentgenogram of the stomach, taken on Nov. 27, 1929.

is normal. A large amount of gastric content is present. The stomach is large and, except for some canalization, its lumen is obstructed in the prepyloric region. After six hours a gastric residue estimated at 50 per cent is present. Diagnosis: Probable carcinoma of the stomach with obstruction" (fig. 1).

*Treatment and Course.*—Because of the gastric retention the patient was put at rest in bed; the stomach was emptied, and a liquid and soft, bland diet was prescribed. On this regimen no further vomiting occurred and the fluid balance was maintained satisfactorily. Two small doses of arsphenamine were given intravenously on December 2 and 5, respectively. Reexamination of the blood on December 3 revealed the hemoglobin to be 93 per cent (Sahli) and the red cells,

4,740,000. The stomach was reexamined roentgenologically on December 5, and described as follows: "A canalized lumen is demonstrable between the cardiac and pyloric regions of the stomach. The pyloric region distal to the deformity appears to be fairly normal. The pylorus and duodenum seem to be normal. A six hour gastric residue estimated at 50 per cent is still present. Diagnosis: Carcinoma of the stomach with obstruction" (fig. 2).

Several intravenous injections of physiologic solutions of sodium chloride and dextrose were given during the two days before operation, and on Dec. 7, 1929, under nitrous oxide, oxygen and ether anesthesia, the patient's abdomen was

Fig. 2.—Roentgenogram of the stomach, taken on Dec. 5, 1929.

explored. The incision was made through the upper part of the rectus muscle on the right side. Except for the stomach no abnormality of any of the intra-abdominal organs was discovered. There were no nodules in the liver and no enlarged lymph nodes except those immediately adjacent to the stomach. Almost the entire distal two thirds of the stomach was greatly thickened and of a rubbery consistency unlike that of carcinoma. One of many enlarged glands along both the lesser and the greater curvature was excised for immediate examination. A frozen section revealed no gross or microscopic evidence of carcinoma.

A resection of the diseased portion of stomach seemed to be advisable. The duodenum was severed at a point just distal to the pylorus, and the lower two thirds of the stomach was resected. The stump of the duodenum was closed, and

the proximal end of the remaining portion of the stomach was anastomosed with the side of a loop of the jejunum which had been brought up through the transverse mesocolon. The mesocolon was sutured about the stomach just proximal to the anastomosis and the abdomen closed without drainage.

The tissue removed at operation was described in the following pathologic report: "The specimen consists of a resected portion of the stomach about 15 x 11 cm., roughly triangular in shape. The wall of the stomach is greatly thickened throughout. On the mucosal surface is a hemorrhagic, ulcerated and scarred area 8 x 6 cm. with irregular, serpiginous and thickened borders. In its margins there are two small, firm areas and one deeper ulcer about 2 cm. in diameter. The

Fig. 3.—Resected portion of the stomach.

attached gastro-hepatic and gastro-colic omental tissue contains several pea-sized lymph nodes that have a rubbery consistency (fig. 3).

"Microscopically the mucosa at the margins of the ulceration shows round cell, plasma cell and polymorphonuclear infiltration with some hemorrhage. Immediately beneath this there are large collections of round cells and plasma cells. The submucosal layer is markedly thickened, and edematous. In it are much fibrous tissue and numerous cellular areas composed of round cells, plasma cells and centrally located epithelioid cells with occasional giant cells. Collections of cells surround many of the arteries imparting a 'signet-ring' appearance. In some instances the arterial lumen is narrowed and in some completely obliterated by endarteritis (fig. 4). The lymph nodes reveal evidences of acute and chronic inflammation with marked hyperplasia of the follicles. Diagnosis: Syphilis of the stomach with ulceration. Lymphadenitis, acute and chronic."

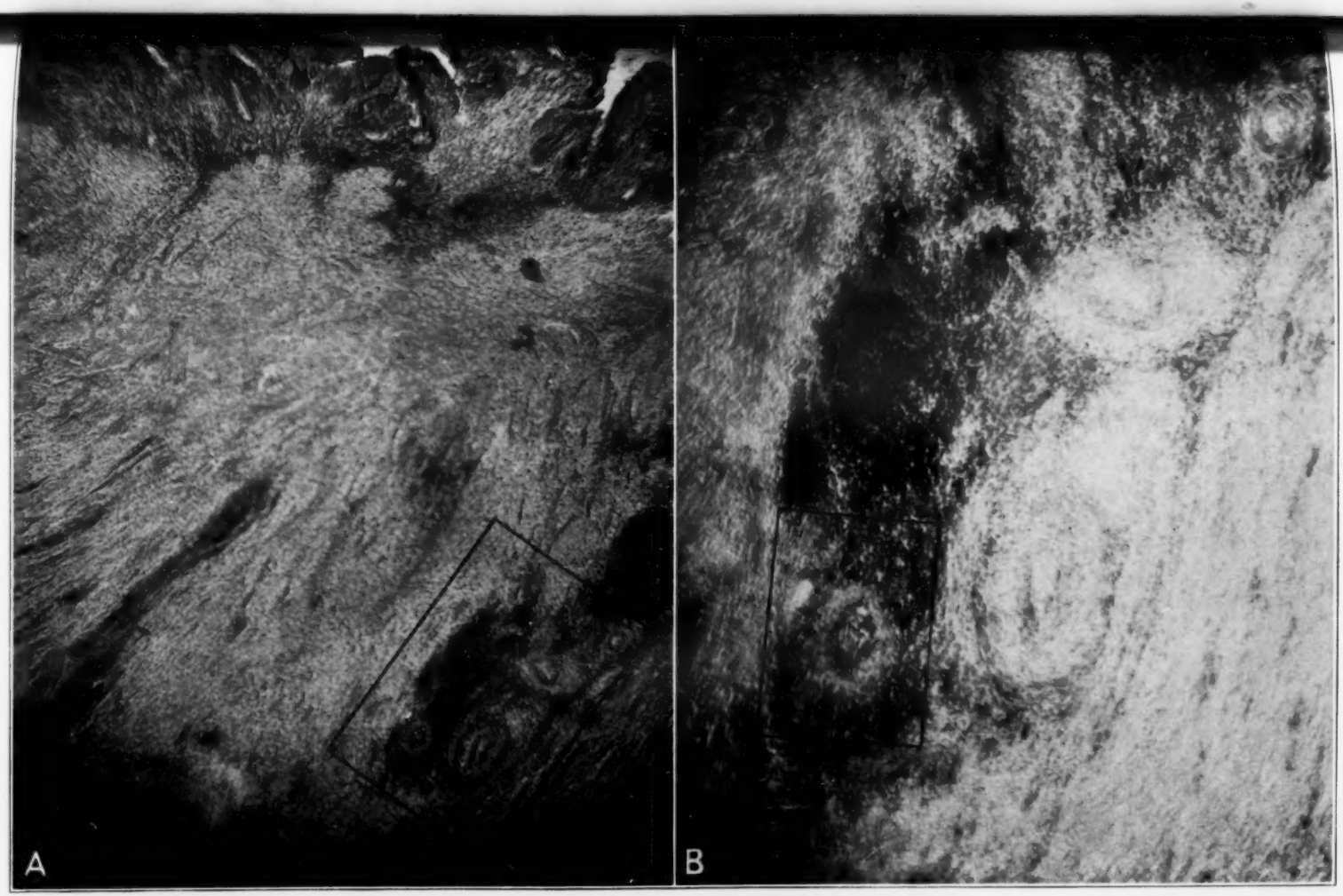


Fig. 4.—*A*, photomicrograph, showing the marked reaction in the gastric wall without ulceration of the mucosa; × 25. *B*, high power view of the portion marked in *A*; × 50.

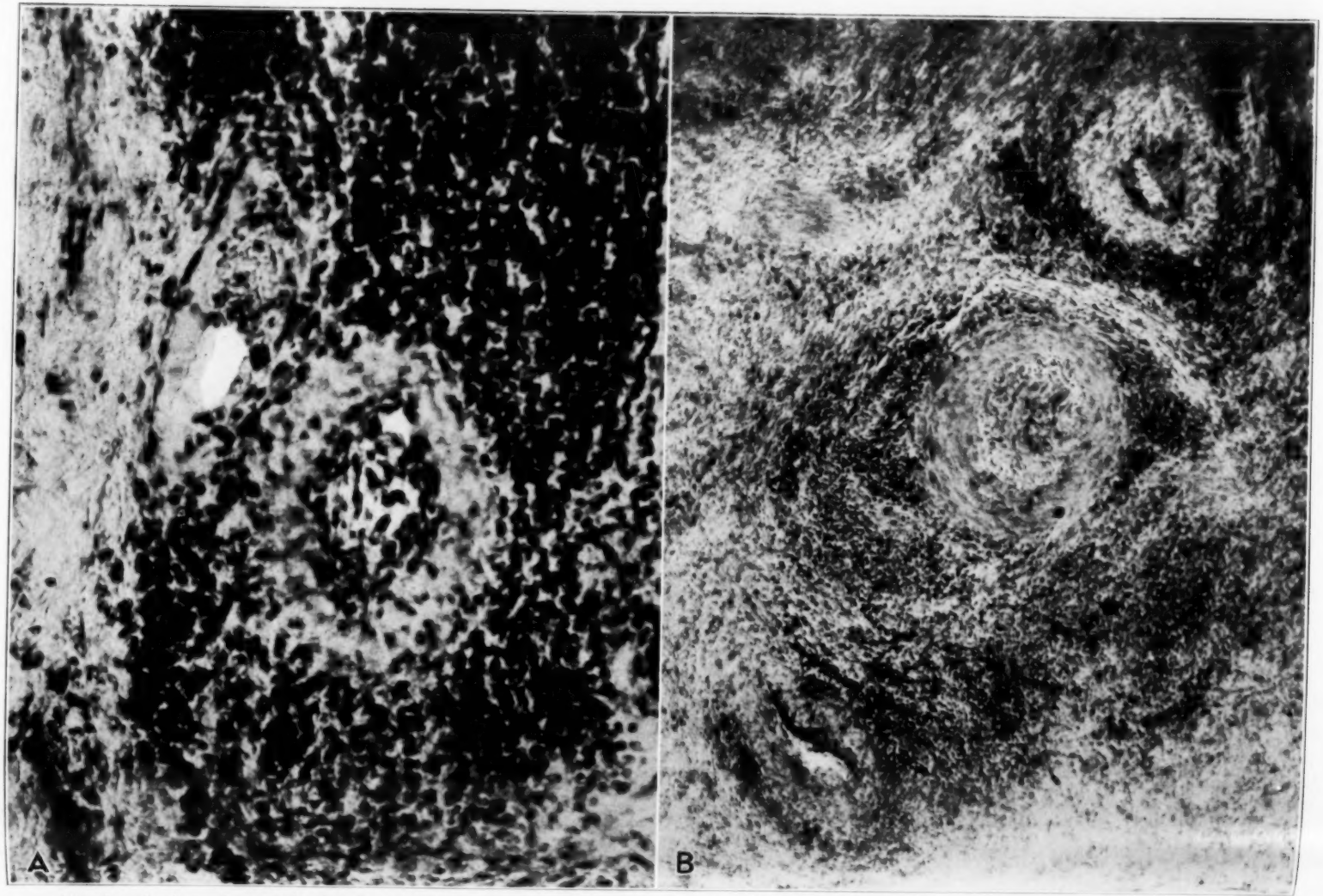


Fig. 5.—*A*, photomicrograph, showing higher power view of the portion marked in figure 4*B*; × 150. *B*, photomicrograph of another area.

Numerous blocks of tissue from various sites in the stomach were studied by the Levaditi technic, but no positively identifiable spirochaeta pallida were discovered.

The postoperative convalescence of the patient was uneventful. He was allowed to go home on Dec. 21, 1929, fourteen days after operation. His condition at that time was excellent. He returned for antisyphilitic treatment periodically for four months, during which time he gained 30 pounds (13.6 Kg.).

A last report from the patient, on March 3, 1931, two years and three months after operation, stated that his general health was excellent, that he had no gastric or other abdominal symptoms and that he was able to carry on his former work without difficulty. He was known to be alive and well on Jan. 1, 1932.

## COMMENT

This case presented many of the clinical and roentgenologic features that have been attributed to gastric syphilis. The histologic characteristics of the portion of stomach removed at operation seem to furnish conclusive proof that the disease was true syphilis of the stomach.

The failure in the search for spirochetes in the tissue was disappointing. In this connection it is impossible to say with certainty what may have been the effect of the preoperative injections of arsphenamine, though it seems likely that they may have caused the disintegration of the spirochetes that might have been present. It might have been worth while to inject some of the tissue into the testis of a rabbit, but this procedure was not thought of until too late. In any similar cases that may be encountered this test will be applied.

## SUMMARY

A brief review of some of the critical literature on syphilis of the stomach has been given. Attention has been called particularly to the histologic criteria employed in making the diagnosis and the necessity of these histologic proofs. A case of syphilis of the stomach encountered at the operation has been described with the histologic proofs of the diagnosis.

Fig. 8.—*A*, photomicrograph, showing higher power view of the portion marked in figure 4*B*. ×80. *B*, photomicrograph of another area

# ADAMANTINOMA

## A CASE OF FIFTY-ONE YEARS' DURATION

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AND

LOUIS STIX, M.D.

NEW YORK

A recent acquisition of the College of Physicians and Surgeons is a large adamantinoma of the lower jaw with a history of fifty-one years' duration. This type of tumor is noted for its slow, persistent growth, but as this history is the longest that we can find on record, the case is presented as one of unusual interest.

Adamantinomas are relatively rare tumors, usually occurring in young people. Grossly they are either solid masses of pale slimy tissue or nodular, part solid and part cystic. They are found within the bone of either the upper or lower jaw, much more frequently in the latter, often in the region of an unerupted tooth, and as they grow cause an expansion of the outer shell of bone. Microscopically, they show a stroma of either adult fibrous tissue or embryonal tissue, similar to that seen in the dental papillae, in which are embedded masses of epithelial cells that approximate the appearance of those of the embryonal enamel organ.

According to Malassez, it is the "epithelial débris" persisting from this organ that is the basis for the tumor. Some of the cells are arranged in sheets, similar to the neck of the primitive organ as it grows down from the alveolar epithelium. Some are in rounded masses similar to the organ itself, the outer cells being arranged radially like the ameloblasts, the inner cells giving a starlike appearance like those of the "stellate reticulum." It is probably the degeneration of these star cells that gives rise to the numerous separate cysts that are frequently found. Occasionally these tumors form teeth. They are slow-growing, difficult to cure, except by radical measures, and apparently may be quiescent for years, as in Porzelt's case, in which the tumor recurred after forty-five years. They rarely metastasize, but exceptional cases with lymph node involvement have been described by Ewing, Simmons and New, and Ewing and Simmons have reported lung metastases.

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From the Laboratories of Surgery, College of Physicians and Surgeons, Columbia University, and the Laboratory of Surgical Pathology, the Presbyterian Hospital.

Fig. 1.—Gross photograph of the inferior aspect of the tumor with the remaining portion of the mandible attached.

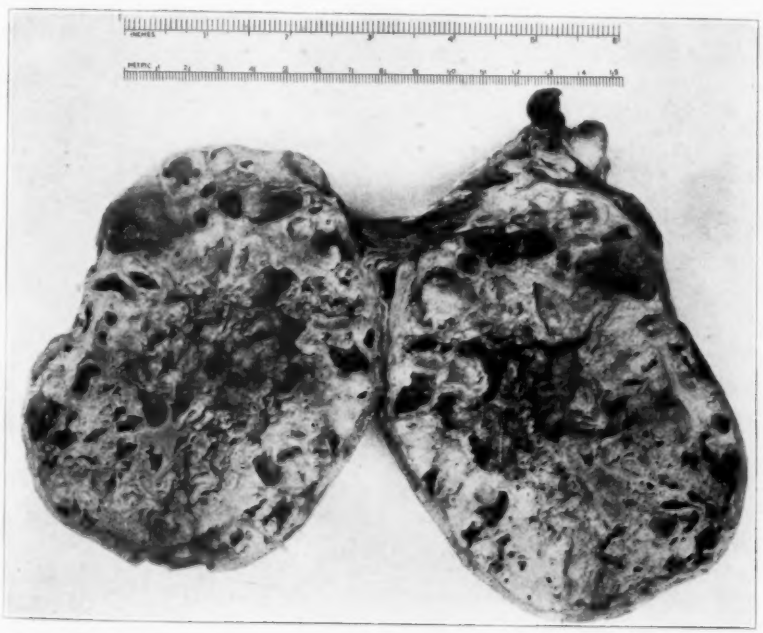

Fig. 2.—Gross photograph of the tumor bisected. Note the necrotic area in the center and the cystic spaces scattered throughout.

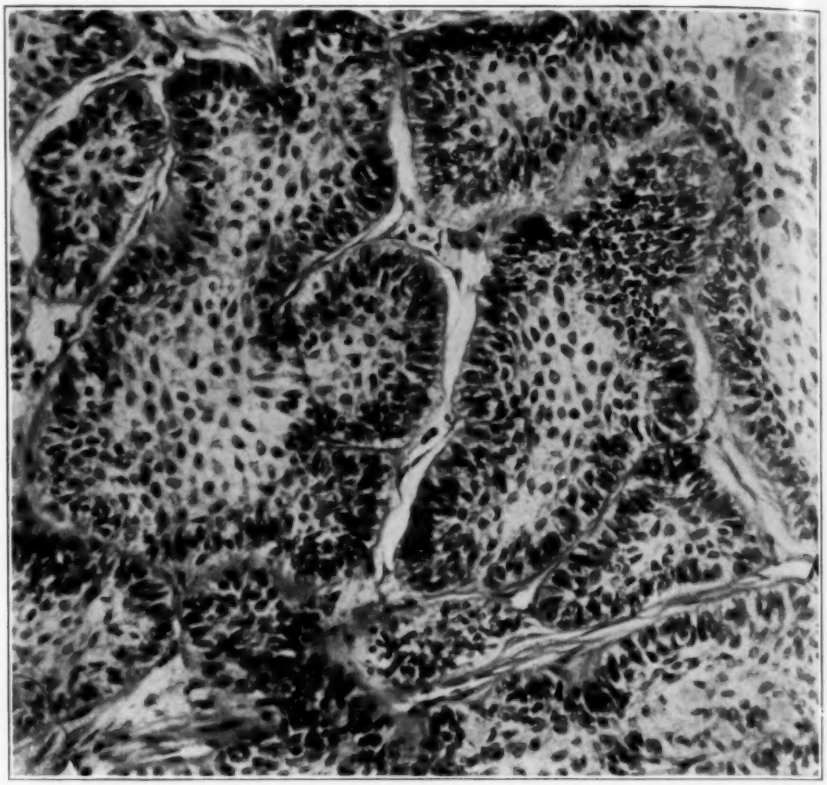

Fig. 3.—Low power photomicrograph showing the typical alveolar arrangement, with connective tissue trabeculae.

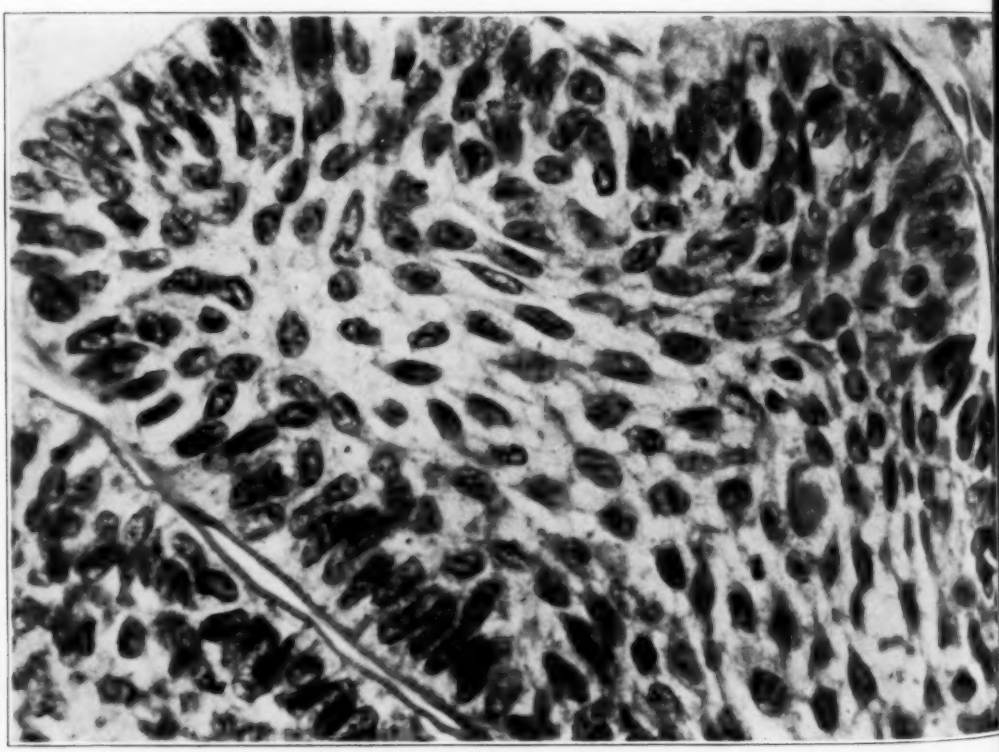

Fig. 4.—High power photomicrograph of the same area as that in figure 3, showing the radially arranged epithelial cells at the periphery of the alveoli and the central cells with intercellular bridges.

REPORT OF CASE

C. M. L., a woman, aged 32, married, was admitted to the Roosevelt Hospital, New York, on June 22, 1885, complaining of a lump in the right side of the lower jaw.

Seven years previously, in 1878, a carious tooth had been extracted, following which the jaw began to swell gradually without pain or tenderness. Four and a half years after the onset the tumor had reached a large size, was circumscribed and limited to the center of the jaw, and hung down so as to touch the shoulder when the head was turned. It was removed surgically at that time, leaving a

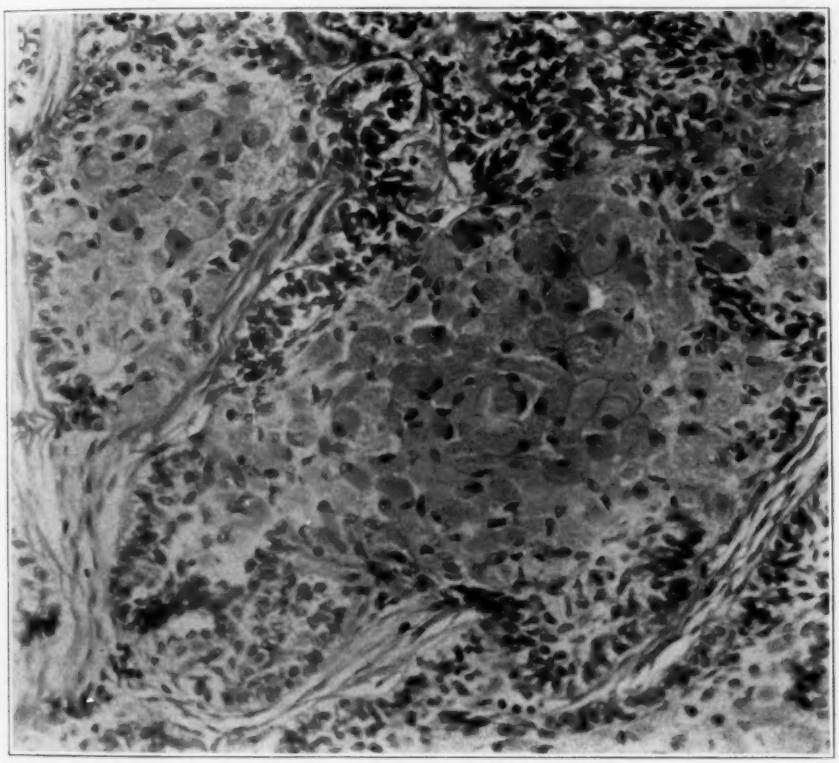

Fig. 5.—Low power photomicrograph showing alveoli in which the central cells have undergone degeneration, probably a precystic phase.

small shell of bone on the lower edge of the jaw and, according to the patient, the source of the tumor on the inner surface. Sequestrums of bone were discharged spontaneously for a year after this operation, and pain began eight months after operation, persisting up to the patient's admission to the hospital. Nine months before admission the pain was somewhat relieved by the surgical drainage of a large abscess situated posterior to the jaw. The tumor steadily increased in size for the nine months previous to admission.

Physical examination on the patient's admission to the Roosevelt Hospital, on June 22, 1885, yielded the following data: "There is a swelling of the lower jaw

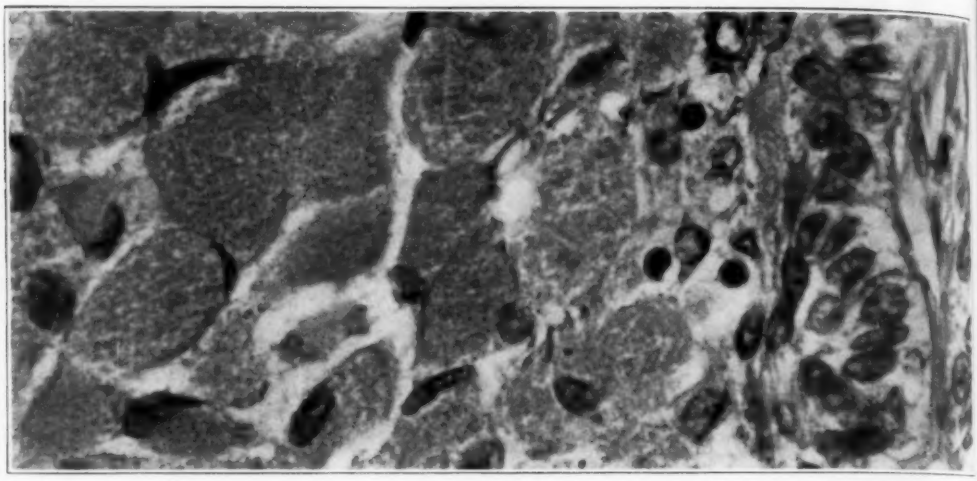

Fig. 6.—High power photomicrograph of the same area as that in figure 5, showing the granular appearance of the cytoplasm in the degenerating cells.

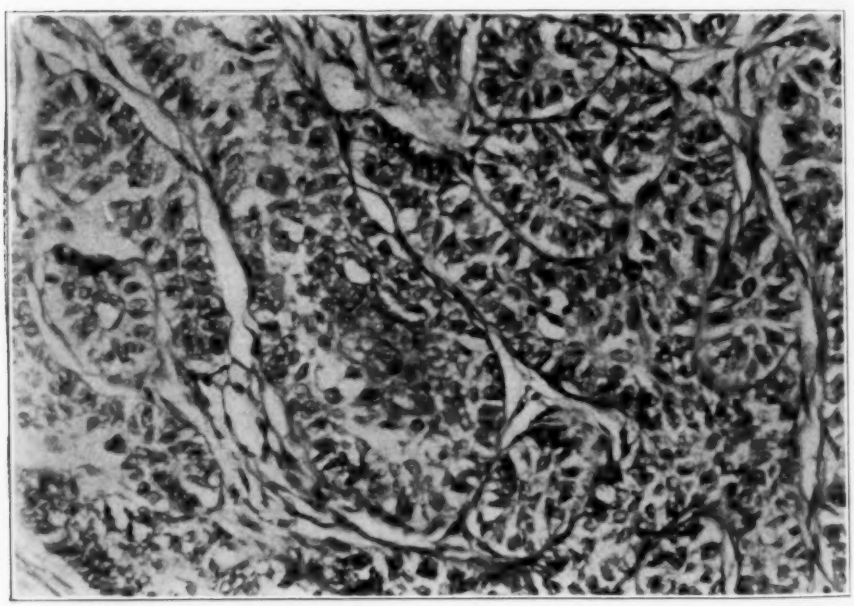

Fig. 7.—Low power photomicrograph showing an area in which the arrangement simulates gland formation.

on the right side of irregular shape, extending from the back of the ramus of the jaw behind and the coronoid process above, downward and forward nearly to the median line and attached to the inferior maxillary bone. It is somewhat coarsely nodular and projects mostly downward and outward. On the inside of the mouth it projects upward above the natural level of the teeth, outward so far as to push out the cheek and somewhat inward so as to slightly displace the tongue to the opposite side. Within the mouth it is lobulated and covered with mucous membrane. The tumor extends back inside the mouth on to the ramus, but cannot be

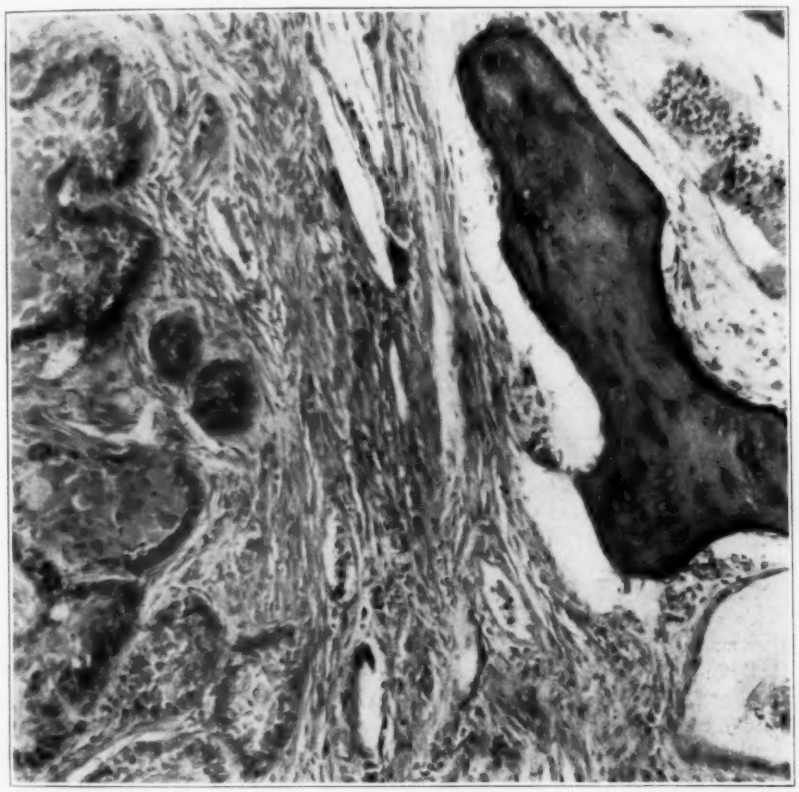

Fig. 8.—Low power photomicrograph showing bone in relation to the tumor.

felt to involve the pharynx at all. The skin over the tumor is not adherent or red. There are no enlarged glands to be felt in the neighborhood and no facial paralysis or dysphagia. There is a constant discharge (worse on lying down), which the patient spits occasionally from the mouth. The discharge comes mostly from two places, posteriorly and anteriorly. Movement of the jaw is not painful."

An operation was performed by Dr. Henry B. Sands[1] on June 23, under ether anesthesia, with antiseptic precautions. The incision was made "from a little below

1. At this time Dr. Sands was professor of the practice of surgery at the College of Physicians and Surgeons, New York.

and anterior to the external auditory meatus, along lower edge of jaw, 1 inch from midline. Dissection down to tumor, which was very vascular. Bleeding controlled. Canine and first bicuspid teeth extracted. Jaw divided at this point, parts along the floor of the mouth dissected (ether being discontinued) away from the tumor, keeping close to bone; coronoid process dissected out; found to be small and imperfect. Joint dissected out; jaw removed." Seventeen days later, the patient was discharged in good condition, signed out by Dr. George S. Huntington, Senior Assistant Surgeon.[2]

In spite of the radical treatment described, the tumor "soon began to grow" again in the left mandible, and it continued to grow almost up to the time of the patient's death in 1929, when she was 76 years old. Six or eight years before her death the tumor had been treated with radium implantations. For two weeks before death the tumor discharged "foul fluid," and during that time it diminished in size. At all times it had been absolutely painless.

An incomplete autopsy was performed in the home by Dr. Frank C. Johnson who was called in after the patient's death and obtained the postoperative history from her husband. At this time the mass was removed with what remained of the left mandible. No secondary masses were found in the vicinity, and there was no suggestion of metastases to thoracic or abdominal viscera. Dr. Johnson presented this unusual material to the laboratory.

In the fixed state the specimen consisted of a rounded mass of firm consistency measuring about 11 by 13 by 14 cm. and weighing 950 Gm. (fig. 1). The greater part of its surface was covered with skin. At one end there was a portion of the condyle and ramus of the lower jaw. There were two ulcerated areas on its lower aspect which led into deep cavities. On cut section (fig. 2) irregular masses of bone extended throughout the specimen. Each cut section revealed a vast number of separate cystlike cavities measuring from 1 to 3 cm. in diameter. Cloudy fluid material and débris were found in these cavities. Throughout the specimen between the cystlike cavities there was solid, more or less homogeneous tissue, except for the center of the tumor, which consisted of a mass of extremely friable foul-smelling débris (figs. 3 to 8).

Microscopically, the specimen showed an alveolar-like structure. There were strands of rather densely packed, dark-staining epithelial cells. There were also larger masses of these cells, the more peripheral ones being columnar and arranged radially in a palisade layer. The central cells of the larger masses were less closely packed and lighter staining. Some of them seemed to be connected with bridges, giving them a roughly stellate appearance. In places these central cells were necrotic, with faded nuclei and cloudy cytoplasm. In others, they had disappeared and left small cystic spaces. The strands and masses of epithelial cells were separated from each other by strands of fibrous connective tissue, some of which contained small spicules of well developed bone. The dark-staining epithelial cells and the central stellate cells resembled closely in both appearance and relationship the ameloblasts and the cells of the stellate reticulum of the embryonal enamel organ.

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# LOBECTOMY AND PNEUMECTOMY IN DOGS

## EXPERIMENTAL SURGERY

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AND
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Our interest in experimental lobectomy and pneumectomy was aroused by the discovery of a safe and reliable method of permanently closing large bronchi.[1] A review of the literature on this subject reveals the appalling mortality of these operations to be due primarily to either pleural infection or reopening of the bronchial stump (or both) subsequent to the operation. The idea at once presented itself that these postoperative complications would be obviated by "closing the stump" before removal of the pulmonary tissue. The results of the experimental investigation of this report bear out this hypothesis.

Pneumectomy was first performed by Rolandus [2] (1492) for the cure of diaphragmatic hernia. However, little attention was given to this field of surgery at that time.

At the beginning of the sixteenth century, Schenk [3] aroused interest in thoracic surgery which subsequently has been kindled by the introduction of apparatus and procedures pertaining to this specialty.

Scientific experimental investigation by Gluck,[4] Marcus,[5] Block,[6] Biondi [7] and others was largely a failure as far as the operations per se were concerned. Of these workers, Biondi's results were most encour-

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1. Adams, W. E., and Livingstone, H. M.: Closing Bronchial Stump in Pulmonary Surgery, Ann. Surg. **95**:106 (Jan.) 1932.

2. Quoted by Murphy, J. B.: Surgery of the Lung, J. A. M. A. **31**:341 (Aug. 13) 1898.

3. Schenk, quoted by Murphy, J. B.: Surgery of the Lung, J. A. M. A. **31**: 151 (July 23) 1898.

4. Gluck, T.: Experimenteller Beitrag zur Frage der Lungenexstirpation, Berl. klin. Wchnschr. **18**:645, 1881.

5. Marcus, quoted by Murphy (footnote 3).

6. Block: Experimentelles zur Lungenresektion, Deutsche med. Wchnschr. **7**: 634, 1881.

7. Biondi, D.: Lungenexstirpation bei experimenteller lokalisierter Tuberculose, Med. Jahrb., 1884, p. 207.

aging. Using rabbits, cats and dogs, he injected tubercle bacilli into the lungs with the hope of producing localized tuberculous lesions. Eleven subsequent total extirpations of one lung were performed, four of the animals dying of pleural infection. Nevertheless, the experiments carried out were of great value in stimulating interest during that period and led to further experimental and clinical investigation.

Kronlein,[2] in 1884, reported two cases in which the apex of the upper lobe was exteriorized and amputated in the treatment for pulmonary tuberculosis. Both cases terminated fatally.

In 1885, Ruggi [2] operated in two cases with a similar result.

However, Tuffier,[2] in 1891, Lawson,[2] in 1893 and Doyen,[2] in 1895, removed small portions of the apex of the right upper lobe in cases of pulmonary tuberculosis with reported favorable results.

Much subsequent experimental work has been reported, the results of which show marked variation. Thus, Murphy,[8] in 1898, did a partial pneumectomy on ten dogs by the exteriorization and amputation method with a mortality of 90 per cent. However, he expressed his belief that this was the procedure of choice in performing that operation. Previous to Murphy's work there had been no reports of total pneumectomy in man.

Meyer [9] performed total excision of a lung in a series of twenty-one dogs with a mortality of 19 per cent. His method included clamping and crushing of the bronchus with subsequent ligation and amputation and burying of the stump with top sutures.

In the experiments of Lilienthal [10] and Joannides,[11] a generous stump was left for closure. Most workers have found it necessary to leave a liberal amount of lung parenchyma to obtain a satisfactory closure of the bronchial stump following pneumectomy.

Bettman's as well as our own studies on the reparative processes of bronchi [12] have demonstrated little or no healing of the bronchus per se other than regeneration of the epithelium; that healing was brought about by peribronchial tissues. Thus Robinson and Sauerbruch [13]

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8. Murphy, J. B.[2]

9. Meyer, Willy: Pneumectomy with the Aid of the Differential Air Pressure, J. A. M. A. **53**:1978 (Dec. 11) 1909.

10. Lilienthal, H.: Thoracic Surgery, Philadelphia, W. B. Saunders Company, 1926, vol. 2, p. 147.

11. Joannides, Minas: Care of the Stump in Pneumectomy and in Lobectomy, Arch. Surg. **17**:91 (July) 1928.

12. Bettman, R. B.: A Study of the Factors Concerned in Failure of the Bronchi to Heal, Arch. Surg. **8**:418 (Jan.) 1924. Adams, W. E., and Livingstone, H. M.: Bronchial Injury and Repair, Ann. Surg. **91**:342, 1930.

13. Robinson, B. S., and Sauerbruch, F.: Untersuchungen über die Lungen-Exstirpation unter vergleichender Anwendung beider Formen des Druckdifferenze Verfahrens, Deutsche Ztschr. f. Chir. **102**:543, 1909; quoted by Bettman.

found that although removal of a single lobe was almost always successful, the reverse was true following complete extirpation of a lung. With differential pressure, the technic was simple, but many dogs died on the sixth to the eighth day of pressure pneumothorax owing to reopening of the stump. Thirty-eight pneumectomies were performed, in only four of which there was recovery.

The following experimental method is presented because of its simplicity of procedure and its very low mortality.

## EXPERIMENTAL METHOD

*Preliminary Stenosis of Bronchus.*—Complete stenosis of the bronchus of the lobe or lobes to be removed is obtained prior to operation. This is produced by cauterization of the entire circumference of the bronchial wall by the application

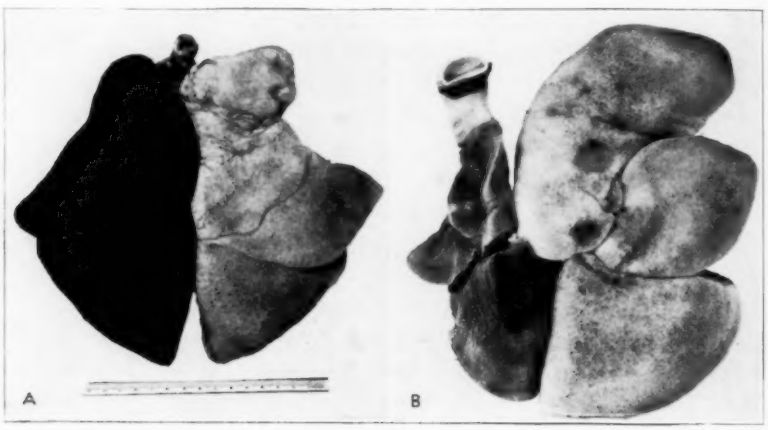


Fig. 1.—*A*, normal lungs showing the relative size of the right and left side. The left lung, shown in black, is collapsed in *B*, and is 100 per cent atelectatic. The right lung in *B* is somewhat hypertrophied.

through a bronchoscope of a 35 per cent solution of silver nitrate. A complete report of this work appears elsewhere.[1] One application usually suffices in bronchi one-half inch (1.27 cm.) or less in diameter. The procedure may be repeated if stenosis is not complete following a single application. The stenosis usually occurs within two weeks following the application of the cautery and is always accompanied by 100 per cent atelectasis of the obstructed pulmonary lobe or lobes (fig. 1, *A* and *B*). When an entire right or left lung is to be removed, the primary bronchus to that side is stenosed.

A diagnosis of complete stenosis of a bronchus, with massive atelectasis of the obstructed lung, is made by endoscopic examination and by the physical findings of dulness to flatness over the side collapsed with the cardiac impulse displaced to that side. These findings are confirmed by fluoroscopic and roentgen examination (figs. 2 and 3).

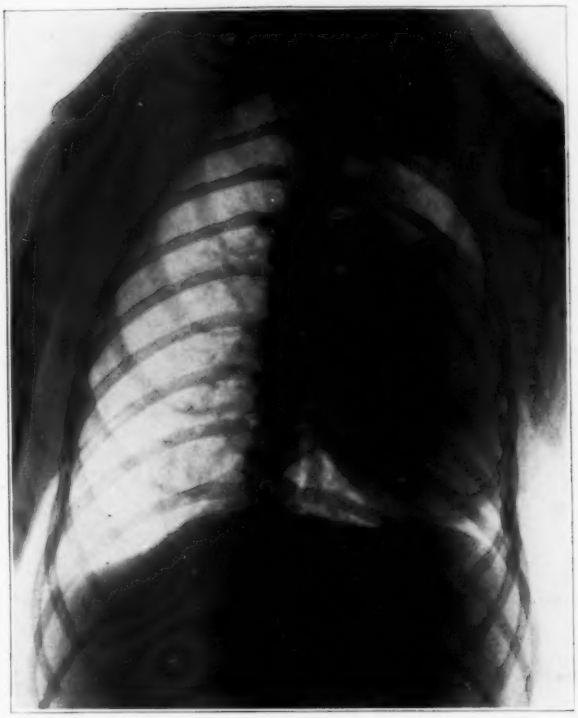

Fig. 2 (dog 837 D).—Roentgenogram of the chest showing massive atelectasis of the left lung following two applications of a 35 per cent solution of silver nitrate to the left primary bronchus. The heart has become displaced and lies against the left thoracic wall. The left side of the diaphragm is also displaced upward.

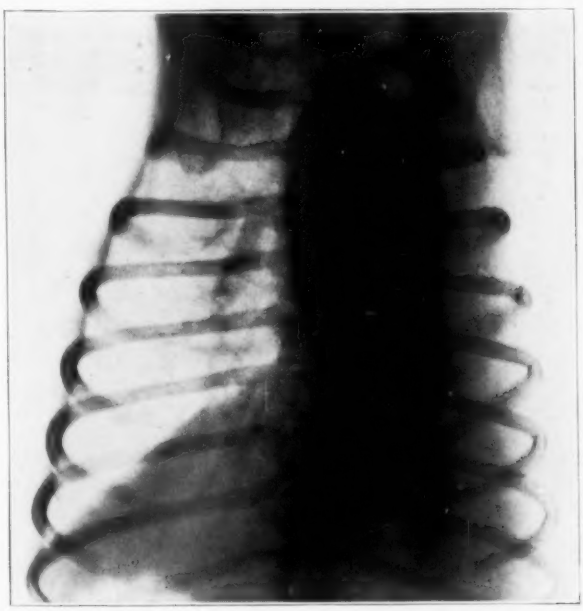

Fig. 3 (dog 400 C).—Roentgenogram of the chest showing massive atelectasis of the right lung. The heart has been displaced against the chest wall and the right side of the diaphragm elevated. Note the dilated bronchi of the remaining inflated lung.

*Removal of Pulmonary Tissue.*—The removal of the pulmonary lobes may be accomplished within a few days to a week subsequent to complete stenosing of the bronchi.

Preliminary to operation, a small dose of morphine and atropine is given. Narcosis is obtained by means of closed ether administration. A complete report by one of us may be found elsewhere.[14] The dog is then placed on the right or left side depending on which pleural cavity is to be entered. The intratracheal tube of the positive pressure ether anesthesia apparatus[14] is now inserted for a depth of 4 or 5 inches (10.16 and 12.7 cm.) into the trachea and the positive pressure mask secured. An air-ether mixture is then administered; however, positive pressure is not yet induced. The thorax is shaved, and the operative field cleansed with tincture of iodine. Sterile drapes are now arranged and careful asepsis observed. An incision 4 or 5 inches in length is made over and paralleling the fifth rib at about its midpoint. About 3 inches (7.6 cm.) of this rib are removed subperiosteally. A small incision is made through the periosteum down to the parietal pleura and the pleural cavity entered bluntly with scissors. The opening is enlarged as the pulmonary lobes become deflated. Positive pressure anesthesia is now begun and regulated so as to obtain only partial inflation of the lungs. With the opening of the pleura, the atelectatic lobes are easily distinguished by their dark bluish-brown color. No pleural exudate is found. The atelectatic lobes are grasped with forceps and mobilized by severing the pleural reflections, following which they are easily lifted up to the surface of the chest. This gives one free access to the vascular supply of the organ. If one entire lung is to be removed, the pulmonary artery to that side is dissected free; two silk ligatures are placed centrally and one distally and the artery is severed between ligatures. If only one pulmonary lobe is to be removed, the pulmonary vessels to that lobe are dissected free, doubly ligated with silk and severed between ligatures. With bleeding thus controlled, the next step consists in isolating each individual lobe bronchus. Each bronchus is dealt with separately in the following manner. A clamp is placed on the bronchus at the edge of the parenchymal tissue, leaving enough space for a chromic catgut ligature proximal to it. This ligature prevents hemorrhage from bronchial vessels. The bronchus is then divided between clamp and ligature. If the division has been made distal to the site of stenosis the air passage will contain a mucogelatinous material, the retained secretion of the bronchial glands. A bare bronchial stump remains, no further care being necessary (figs. 4 and 5).

The wound is now closed in layers under as much positive pressure as is necessary to inflate the remaining lobes to as nearly fill the chest cavity as possible. A running stitch of catgut is used to close the pleura, muscles and subcutaneous tissue. An intracutaneous stitch of catgut is also used preceding closure of the skin by interrupted silk sutures. The wound is dressed and sealed with collodion, and the dog removed to its quarters.

*Postoperative Course.*—During the first two days the animal eats little or nothing and appears somewhat weak. It lies quietly in its cage most of the time. By the third or fourth day, however, it is up and walking about a great deal. It eats well and appears to be gaining strength quite rapidly. At the end of a week, it appears entirely well. Most dogs exhibited a nonproductive cough during the first four or five days following operation. All of the wounds closed in the described manner, remained clean and healed by primary union.

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14. Livingstone, H. M., and Hrdina, L. S.: A Modified Meltzer Apparatus for Anaesthesia in Animals, J. Lab. & Clin. Med. **16**:74, 1930, fig. 3.

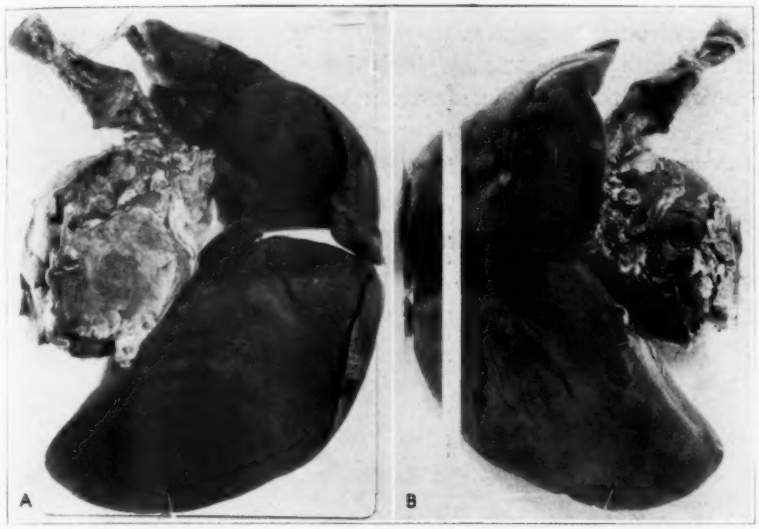


Fig. 4.—*A* and *B*, views of the heart and left lung of a dog killed following pneumectomy of the right lung. View *B* shows the bronchial stump remaining after pneumectomy.

Fig. 5.—*A* and *B*, views of the lungs. The small atelectatic right lung was removed at operation. Note the contrast in size and color to the larger left lung which was removed at time of autopsy. *B* shows the bronchial stump remaining after pneumectomy of the right lung.

RESULTS

One or two lobes were removed in twenty dogs without a single death. All pulmonary lobes on one side were extirpated in eight dogs with the death of one animal. This dog died of respiratory failure on the operating table as the operation was completed, due to defective tubing in the positive pressure apparatus. A careful preoperative check of the apparatus would have obviated this accident. Of the remaining

Fig. 6 (dog 795 C).—Roentgenogram of the chest taken six months following the removal of the right lower and accessory pulmonary lobes, and three weeks following pneumectomy of the left lung. Note the heart and trachea drawn far to the left with elevation of the left side of the diaphragm. The remaining two right lobes exhibit compensatory emphysema, being hyperinflated to fill the thoracic cavity.

seven, two have had a subsequent lobectomy performed on the opposite side, two lobes being removed in each dog. Both dogs had an uneventful convalescence. Thus a total of thirty operations have been performed on twenty-eight dogs without a single death due to the procedures per se (fig. 6). Dogs killed from two months to a year following the foregoing procedures presented no fluid in the pleural cavities. A small number

of adhesions were found in the region of the amputation stump. The remaining pulmonary tissue exhibited varying degrees of compensatory emphysema (fig. 7). Electrocardiograms prior to the death of the animals deviated very little from the normal.

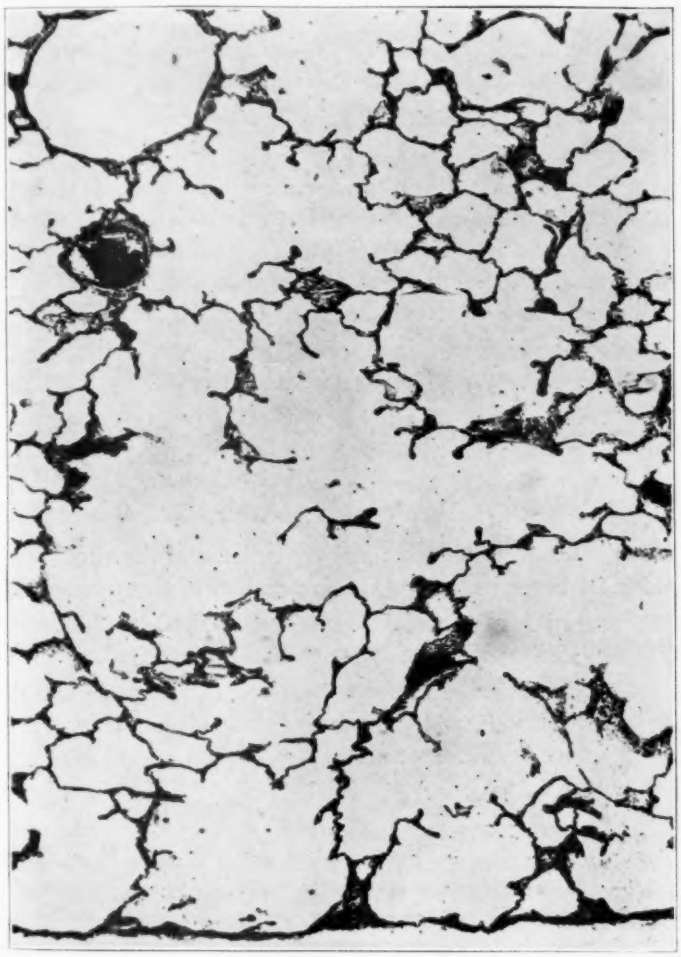

Fig. 7.—Photomicrograph of inflated pulmonary tissue of a dog killed several months subsequent to pneumectomy of an atelectatic right lung, showing marked emphysema.

## COMMENT

The preliminary production of a complete stenosis of the pulmonary lobe bronchus preceding lobectomy was simple and accompanied by no mortality when a solution of silver nitrate of 35 per cent or less was employed. By using this procedure, danger of pleural infection or

pneumothorax following the subsequent amputation of the pulmonary lobes was obviated, an air-tight closure of the bronchial stump having been produced prior to removal of the pulmonary lobe. Thus, there is no dependence on popostoperative healing to produce an air-tight closure of the bronchial stump as is the case in operations in which the stump is closed subsequent to removal of the pulmonary tissue. Postoperative pleural infection and pneumothorax having thus been obviated, the mortality accompanying the procedure was practically nil.

No postoperative complications arose due to reopening of a stenosed bronchial lumen.

During the operation, hemostasis was readily obtained, and the pulmonary lobes were easily removed owing to their having shrunk down to the atelectatic condition. Complete pneumectomies were performed in from twenty to thirty minutes, and the subsequent removal of a lobe on the opposite side was accompanied with equal ease and success.

This procedure is being made use of at the present time in studies on the cardiorespiratory physiology of bilateral subtotal pneumectomized dogs.

Preparations are being made to test its clinical application.

## CONCLUSIONS

The simplicity of preparation and execution and the exceedingly low associated mortality are the remarkable features of this operation.

It has proved highly satisfactory in experimental investigations; however, its clinical application is yet to be demonstrated.

The usual difficulties of associated pneumothorax and pleural infection have been obviated, and thus the greatest obstacles in performing pneumectomy have been overcome.

## PROTOCOL

Dog 795 C.—The dog weighed 11.5 Kg. Complete stenosis of the right lower and accessory lobe bronchi was produced. This was accompanied by massive atelectasis of these two lobes. The removal of these two lobes was carried out a few weeks later. Three months subsequent to this the left primary bronchus was completely stenosed and the left lung collapsed. Pneumectomy of the left lung was performed several months later. The dog is healthy and active at the present time, four months following the last operation; 23.7 per cent of the original pulmonary tissue remains.

July 3, 1930: The dog was given a prebronchoscopic dose of morphine of ¼ grain (16 mg.) per kilogram of body weight. One and one-half hours later, bronchoscopy was performed and the right accessory lobe bronchus cauterized with a 35 per cent solution of silver nitrate. The dog was quiet for a few days and exhibited a nonproductive cough.

July 15: Bronchoscopy was carried out as described. The accessory lobe bronchus was completely stenosed. The right lower lobe bronchus was cauterized with a 35 per cent solution of silver nitrate. A postbronchoscopic course similar to that described, followed.

August 22: Bronchoscopy revealed complete stenosis of the right lower lobe bronchus.

August 26: Lobectomy of the right lower and accessory lobe bronchi was performed.

A preoperative dose of morphine, 0.015 Gm., and atropine, 0.0004 Gm., was given. Under intratracheal ether anesthesia, an incision was made over and paralleling the right sixth rib. The right pleural cavity was entered bluntly through the fifth interspace and positive pressure anesthesia begun as the thoracic contents fell away from the chest wall. The atelectatic lobes (right lower and accessory) were easily recognized by their color. The branch of the pulmonary artery to the right lower lobe was dissected free, two ligatures of silk placed centrally and one distally and the artery divided between ligatures. This also cut off the blood supply to the accessory lobe. The several veins leading from the two lobes to the left auricle were dealt with in a similar manner. The bronchus of each lobe was clamped individually, just proximal to the lung parenchyma. A silk ligature was placed proximal to the clamp to control bleeding of the bronchial vessels and the bronchi each divided between clamp and ligature. As the bronchi were divided, a mucogelatinous material was seen signifying that the division was distal to the site of stenosis. No further care was given the bronchial stump. The remaining lung tissue was inflated by increasing the positive pressure so that the entire thoracic cavity was filled by its contents. The wound was closed in layers under positive pressure, using heavy braided silk to retain the fifth and sixth ribs in close approximation. Catgut was used for the muscle and subcutaneous tissues, an intracutaneous suture of catgut also being used. The skin was closed with interrupted silk and a collodion dressing applied. The dog was returned to its quarters in good condition.

August 27: The dog lay quietly in its quarters and refused food. An occasional nonproductive cough was exhibited.

August 29: The dog walked about and appeared to be improving.

August 31: The dog appeared entirely well except for an occasional nonproductive cough. The wound had healed by primary intention.

October 9: Bronchoscopy was performed. The right lower and accessory lobe bronchi appeared as before. The left primary bronchus was cauterized with a 35 per cent solution of silver nitrate. The usual postbronchoscopic course followed.

October 29: Bronchoscopy was carried out as previously described. The left primary bronchus was completely stenosed. On physical examination, the left side of the chest was flat to percussion. Fluoroscopy and roentgen examination disclosed the heart drawn against the left thoracic wall and massive atelectasis of the left lung.

April 23: Pneumectomy of the left lung was performed. A preoperative dose of morphine, 0.015 Gm., and atropine, 0.0004 Gm., was given.

Under intratracheal ether anesthesia an incision was made over the left fifth rib, and 3 inches of this rib was removed subperiosteally. The left pleural cavity was entered bluntly and positive pressure anesthesia begun as the thoracic contents fell away from the wound. The heart was found to lie directly beneath the incision, and the left lung was 100 per cent atelectatic. The left pulmonary artery was

dissected free, two ligatures placed centrally and one distally and the artery severed between ligatures. The several veins leading from the two lobes were dealt with in like manner. The left upper lobe bronchus was clamped near the parenchyma of the lobe, and a ligature was placed proximal to the clamp to control bronchial bleeding. The bronchus was divided between clamp and ligature. The left lower lobe bronchus was treated in a similar manner.

The remaining lung was inflated by increasing the positive pressure so that almost the entire thoracic cavity was filled by its contents.

The wound was closed in layers under positive pressure and a dressing applied.

April 24: The dog lay quietly in its quarters and refused food. An occasional nonproductive cough was exhibited.

April 26: The dog appeared to be improving. It walked about and took both food and water.

April 28: The dog appeared entirely well except for an occasional nonproductive cough. It was quite active. The wound had healed by first intention.

May 3: The dog appeared normal. No cough had been present during the past two days.

# INTERNAL HERNIA

## THREE ADDITIONAL CASE REPORTS

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The subject of internal hernia is one that surgical textbooks have largely neglected. Although Watson, in his volume on hernia, devoted a chapter to the subject, and H. B. Stone also mentioned internal hernias in some detail, in many instances but little attention is paid them. They are comparatively rare, but for that very reason are important since their rarity makes their diagnosis difficult.

By the term internal hernia is meant a protrusion into pouches or openings in the peritoneum in contrast to hernias through defects in the retaining walls of the abdomen. There are many varieties. Watson classed as most common those of the duodenal fossae described by Eppinger, Treitz and Landzert: the pericecal, the intersigmoid and those through the foramen of Winslow. Stone said that the most frequent are those about the duodenojejunal junction: the cecum, the mesentery of the sigmoid and through the foramen of Winslow.

Short gave seven common types of internal hernia: the left and right paraduodenal, the retrocolic, the ileo-appendicular, those through the foramen of Winslow, the intersigmoid and those through the transverse mesocolon. The eleven other cases given are in locations too infrequent to deserve separate classification. Stangl divided retroperitoneal hernia into duodenal, pericecal, intersigmoid and hernia through the foramen of Winslow. This is a classification with which Lower and Higgins agree.

The classification of internal hernia is not, as a matter of fact, without confusion. In looking over the literature it is found that some authors use the term retroperitoneal hernia without further division. This use is too general, for the term retroperitoneal hernia covers a large field and includes many of the internal hernias. Others use this term interchangeably for the hernia of Treitz, a classification that Short does not use. No doubt he placed this type of hernia in the paraduodenal group, since the fossa occurs just at the end of the duodenum. Garber uses the term interchangeably for the duodenojejunal variety. His cases have been classed under hernia of Treitz. Watson, however, listed duodenojejunal hernia as a separate class and wrote that it is

rarely associated with any other variety of duodenal fossa. It is exposed by pulling the transverse colon upward and the jejunum downward and to the right.

To a large extent the classification of Short has been adhered to in this paper. This has simplified comparison of reports of internal hernia in the literature from 1925 to July, 1931 (the period covered here), with those reported by him in 1925. The cases of hernia of Treitz, classed definitely by the authors under this heading, should be placed under the paraduodenal group. In addition, space has been given for recording unclassified retroperitoneal hernias, for duodenojejunal hernias and for paraduodenal hernias in which the side involved is not stated.

It is my opinion that the best classification of retroperitoneal hernia is paraduodenal (right and left and duodenojejunal groups), paracecal, intersigmoid and hernia through the foramen of Winslow. Internal hernias should include this group of retroperitoneal hernias, together with hernias into anomalous openings, such as, through the mesentery (transverse mesocolon, etc.), through the omentum and into or through the broad ligament.

*Classification of Internal Hernias*

- Retroperitoneal
  - Paraduodenal
    - Right
    - Left
    - Duodenojejunal
      - Superior
      - Inferior
  - Paracecal
    - Ileocecal
    - Retrocecal
    - Ileocolic
  - Intersigmoid
  - Foramen of Winslow
- Anomalous openings
  - Through the mesentery
  - Through the omentum
  - Through or into the broad ligament

In 1925, Short reviewed the literature on internal hernia, bringing the case reports up to date. While no attempt has been made to cover the same ground, and only cases reported in the American, English, German and French literature have been looked up, yet in the course of this search certain omissions to his bibliography have been discovered. Thus Short, reporting the case of Copenhaver of internal hernia through the foramen of Winslow, omitted from his summary the ileocecal hernia and the hernia through the omentum, both of which are given in the same paper. The case of Bryan of duodenojejunal hernia is not reported. He mentioned Andrew's article but did not include the case of paraduodenal hernia reported there. Nor did he give the case of Ullman, nor Radovan's case which Ullman quotes.

Other authors have also reported cases that he missed. The case of Pringle of a girl 5 years old, the case of Coffey, the case of Crymble—all reported by Heaney and Simpson—are not included in Short's paper. Dewis and Miller, in their discussion of hernia through the foramen of Winslow, noted several cases that Short missed. Garber reported two cases of hernia of Treitz, reported since Short's paper, but not included in my bibliography. All these cases are given in table 1.

TABLE 1.—*Cases Omitted by Short*

| Author | Type of Hernia | Result |
|---|---|---|
| Quoted by Dewis and Miller: | | |
| Delangenier, 1924 | 1 through foramen of Winslow | Not given |
| Corry, 1924 | 1 through foramen of Winslow | Reduction with recovery |
| Ullman, 1924 | 1 through foramen of Winslow | Enterotomy with death |
| quotes Radovan, 1919 | 1 through foramen of Winslow | Enterotomy with recovery |
| Garber quotes: | | |
| Kuschewa and Malenowsky | 1 hernia of Treitz | Not given |
| Jefeth | 1 hernia of Treitz | Not given |
| Heaney and Simpson quote: | | |
| Pringle | 1 through transverse mesocolon | Not given |
| Coffey | 1 through transverse mesocolon | Not given |
| Crymble | 1 through transverse mesocolon | Not given |
| Copenhaver, 1923 | 1 ileocecal | Enterostomy with death |
| | 1 through omentum | Resection with death |
| Andrews, 1923 | 1 paraduodenal | Hole sutured; result not given |
| Bryan, 1920 | 1 duodenojejunal | Reduction; enterojejunostomy recovery |

TABLE 2.—*Total Number of Cases of Internal Hernia*

| Type of Hernia | Short 1915–1925 | Omitted by Short | 1925–1931 | Total |
|---|---|---|---|---|
| Retroperitoneal unclassified | .. | .. | 2 | 2 |
| Paraduodenal | | | | |
| Duodenojejunal | .. | 1 | 3 | 4 |
| Treitz | .. | 2 | 6 | 8 |
| Side unstated | .. | 1 | 1 | 2 |
| Left | 43 | .. | 5 | 48 |
| Right | 5 | .. | 4 | 9 |
| Paracecal | | | | |
| Retrocolic | 17 | .. | 4 | 21 |
| Ileo-appendicular | 5 | 1 | 2 | 8 |
| Foramen of Winslow | 24 | 4 | 7 | 35 |
| Intersigmoid | 8 | .. | 4 | 12 |
| Through transverse mesocolon | 17 | 3 | 8 | 28 |
| Others | 11 | 1 | 14 | 26 |
| Totals | 130 | 13 | 60 | 203 |

In this paper fifty-seven more cases have been culled from the literature, and 3 personal cases are reported. This brings the total up to two hundred and three. In table 2 these have been summarized according to the location of the hernia, and added to previous total reported cases.

## REPORT OF CASES

The three cases from my personal record are given here.

CASE 1.—H. D., a man, aged 43, was seen with acute pain in the upper abdominal region, shock and vomiting approaching the fecal type. The previous history elicited stabbing pain in the epigastrium and upper left side of the abdomen,

associated with vomiting. These attacks lasted from two to three days and were preceded by attacks of constipation. The symptoms were of four years' duration, with attacks becoming more frequent. General examination revealed a well built and well nourished man. The abdomen was of the semibarrel type. There was no visible or palpable mass on pulsation. There was slight tenderness in the epigastrium and gas distention. The preoperative diagnosis was intestinal obstruction or pancreatitis. Operation, with the patient under ethylene and ether, revealed a membranous pocket extending from mesenteric attachment of the vertebra to the left side of the abdominal wall, producing a pouch of the left paraduodenal type with opening 1½ inch in diameter. This pouch contained all the jejunum and 6 feet of the ileum. About 6 ounces of serosanguineous fluid escaped. The intestines were removed from the pouch, and the membranous band was incised, the hernial sac being destroyed. The recovery was good. The appendix had been removed previously.

Case 2.—B. X., a woman, aged 29, gave a history of bloating and much gas after meals, especially after eating beans. Appendectomy had been performed several weeks before by another surgeon without relief. No doubt the hernia was overlooked at this operation. There was no vomiting. Her physician gave her castor oil, and she had a dozen small bowel movements. Examination revealed a bulge to the left of the umbilicus the size of a grapefruit. Peristalsis was normal. The preoperative diagnosis was abdominal tumor.

At operation the small intestine was not visible free in the abdomen, and it was observed under the peritoneum. The greater part of the small bowel had herniated through an opening into a pouch, causing partial obstruction. There was some lymph exudate at the cecal region, and all the small intestines were highly congested after delivery from the sac. The hernia was of the left paraduodenal type. The peritoneal holes were sutured, and the patient went into shock. The incision was closed. There was a gradual recovery.

Eleven years later the patient was seen for lacerated cervix and perineum, retroversion of the uterus with some prolapsus. In the course of operation the small intestine was found matted together with many adhesions. The omentum was free, but the bowel was adherent to the upper end of the incision. The bladder was adherent to the uterus. The region of the former hernial opening was found to be closed and covered with scar tissue. The upper portion of the abdomen was completely sealed off with adhesions. Recovery was good.

Case 3.—A. Z., a man, aged 26, had undergone posterior gastro-enterostomy, performed three weeks previously for duodenal ulcer by another surgeon. For two weeks the patient vomited green material and suffered from pain and colic. The preoperative diagnosis was vicious circle or obstruction. Operation revealed the small bowel in the lesser peritoneal cavity, through the transverse mesocolon where it had not been fixed to the stomach. The hernia was reduced and the opening sutured. Good recovery followed.

## REVIEW OF LITERATURE

The sixty cases of internal hernia reported since 1925, including the foregoing three cases, up until July, 1931, are listed in table 3 alphabetically according to the author and the type of hernia. The totals at the bottom of this table correspond to the totals in the third column in table 2.

In table 4 the cases are again listed alphabetically according to authors, and further data: sex, age, symptoms, type of operation, result, etc., have been tabulated.

TABLE 3.—*Classification of Cases of Internal Hernia Reported Since 1925*

| Author | Retroperitoneal Unclassified | Paraduodenal | | | | | Through Mesentery | | | | | Others |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Duodeno-jejunal | Hernia of Treitz | Side Not Stated | Left | Right | Paraceeal | Foramen of Winslow | Intersig-moid | Through Mesocolon | Location Not Stated | |
| Aigrot, 1930 | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | |
| Brown, 1929 | .. | 1 | .. | .. | .. | .. | .. | .. | .. | .. | .. | |
| Cabot, 1927 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | |
| Carling, 1926 | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | |
| Christophe, 1926 | .. | .. | 2 | .. | .. | .. | .. | .. | .. | .. | .. | |
| Coley and Hoguet, 1929 | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | |
| Deaver and Burden, 1929 | .. | .. | .. | .. | .. | 1 | .. | 1 | .. | .. | .. | |
| Debray, 1929 | .. | .. | 1 | .. | .. | .. | .. | .. | .. | .. | .. | |
| Dewis and Miller, 1927 | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | |
| Donald, 1930 | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | |
| Eitel, 1926 | .. | .. | .. | .. | 1 | .. | .. | .. | .. | .. | .. | |
| Elston, 1926 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | |
| Erdély, 1927 | .. | 1 | .. | .. | .. | .. | .. | .. | .. | .. | .. | |
| Folliasson, 1931 | .. | .. | 1 | .. | .. | .. | .. | .. | .. | .. | .. | |
| Garber, 1928 | .. | .. | 1 | .. | .. | .. | .. | .. | .. | .. | .. | |
| Gibby, 1928 | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | |
| Godard and Smith, 1929 | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | |
| Green, 1927 | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | |
| Hamilton, 1926 | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | |
| Heaney and Simpson, 1925 | .. | .. | .. | .. | .. | .. | .. | .. | .. | 2 | .. | |
| Hennig, 1926 | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | |
| Jackson, 1930 | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | |
| Janes, 1929 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 2 broad ligament |
| Judd, 1929 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | |
| Koch, 1926 | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | |
| Kostlé, 1927 | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | |
| Lefèvre, 1927 | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | |
| Liebers, 1926 | .. | .. | 1 | .. | .. | .. | .. | .. | .. | .. | .. | |
| Long, 1929 | 1 | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | |
| Lower and Higgins, 1925 | .. | .. | .. | .. | 1 | 1 | .. | .. | .. | .. | .. | |
| Malcomb, 1927 | .. | 1 | .. | .. | .. | .. | 1 | .. | .. | .. | .. | |
| Martzloff, 1930 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 omentum |
| Masson, 1930 | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | .. | |
| McCarthy, 1926 | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | |
| Muller, 1928 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | |
| Nel, 1929 | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | |
| Odermatt, 1926 | .. | .. | .. | .. | .. | .. | .. | .. | .. | 1 | .. | |
| Siegmund, 1927 | .. | .. | .. | .. | .. | .. | .. | .. | .. | 3 | .. | |
| Stangl, 1930 | .. | .. | .. | 1 | .. | .. | .. | .. | .. | .. | .. | |
| Steinke, 1931 | .. | .. | .. | .. | 2 | .. | .. | .. | .. | 1 | .. | |
| Sumner, 1929 | 1 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | |
| Thevenard, 1928 | .. | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | |
| Traum, 1931 | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | |
| Turner and Scholefield, 1930 | .. | .. | .. | .. | 1 | .. | .. | .. | .. | .. | .. | |
| Venables, 1930 | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | .. | |
| Vidgoff and Stureon, 1930 | .. | .. | .. | .. | .. | .. | 1 | .. | .. | .. | .. | |
| Watschugoff, 1931 | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | .. | 3 fovea supra-vesicalis |
| Total, 60 | 2 | 3 | 6 | 1 | 5 | 4 | 7 | 7 | 4 | 11 | 4 | 6 |

In table 5 is compared the mortality of the cases listed from 1925 to 1931 with the mortality given by Short.

From these tables and the material from which they are drawn certain interesting facts come to light.

TABLE 4.—*Cases of Internal Hernia Reported Since 1925*

| Author | | Sex | Age | Symptoms | Preoperative Diagnosis | Operation | Type of Hernia | Results | Comment |
|---|---|---|---|---|---|---|---|---|---|
| Aigrot, 1936..... | | M | 67 | Stomach trouble for 20 yrs.; acute pain in epigastrium; vomiting for 24 hrs. | Perforated ulcer of stomach | Reduction | Foramen of Winslow | Recovery | |
| Brown, 1929..... | | .. | .. | Symptoms of obstruction; abdominal pain; vomiting | Acute intestinal obstruction | Reduction; jejunotomy | Duodenojejunal | Recovery | |
| Cabot, 1927..... | | M | 30 | Acute abdominal pain; collapse | Diffuse peritonitis; obstruction | End-to-end anastomosis | Through mesentery | Recovery | Two operations |
| Carling, 1926..... | | M | 27 | Acute abdominal pain | Gastric ulcer | Reduction | Foramen of Winslow | Recovery | ..... |
| Christophe, 1926..... | (*a*) | M | 37 | Gastric symptoms for 5 yrs.; colic, vomiting, tumor for 6 wks. | Not made | Reduction; duodenojejunostomy | Treitz | Death | Hernia not recognized at first operation; death from laryngitis |
| | (*b*) | M | 63 | Symptoms of intestinal obstruction | Not made | Celiotomy | Treitz | Death | Autopsy showed hernia |
| Coley and Hoguet, 1929. | | M | 39 | Occasional abdominal pain for 6 mos. | Retroperitoneal | Reduction | Retrocolic | Recovery | Roentgenogram negative |
| Deaver and Burden, 1929 | (*a*) | M | 27 | Sudden onset; pain in upper portion of abdomen; vomiting, gastric symptoms several years | Not made | Reduction | Foramen of Winslow | Recovery | ..... |
| | (*b*) | M | 25 | Severe pain in abdomen; vomiting for 2 days; several previous attacks | Subsiding appendicitis | Reduction | Right paraduodenal | Recovery | ..... |
| Debray, 1929..... | | F | 63 | History of alternate diarrhea and constipation; vomiting | Terminal generalized peritonitis | None | Treitz | Death | Autopsy showed hernia and peritonitis |
| Dewis and Miller, 1927... | | F | 42 | Pain in epigastrium for 20 days; another attack 2 wks.; vomiting | Perforated peptic ulcer of cholecystitis | "Tumor" found and drained | Foramen of Winslow | Death | Autopsy showed hernia |
| Donald, 1930..... | | M | 57 | Abdominal pain for 4 days; vomiting | Acute obstruction | Reduction | Paracecal | Death | Death 2 hrs. after operation |
| Eitel, 1926..... | | M | .. | Digestive disturbances for years | Acute appendicitis | Reduction; jejunostomy | Left paraduodenal | Recovery | ..... |
| Elston, 1926..... | | F | 16 | Sudden onset of abdominal pain, nausea, vomiting; previous attack 4 mos. ago | Not made | End-to-end anastomosis | Through mesentery | Recovery | Reduction impossible; congenital aperture |
| Erdély, 1927..... | | M | 31 | Fever, constipation, vomiting, cramps for 8 mos.; tumor-like mass for 3 wks. | Hernia | Reduction | Duodenojejunal | Recovery | ..... |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Folliasson, 1931..... | | M | 21 | Nausea, vomiting, gastric distress; symptoms of obstruction | Obstruction; tuberculosis? | Reduction | Treitz | Recovery | Roentgenogram showed obstruction |
| Garber, 1928..... | | M | 62 | Severe pain in abdomen; similar attacks 20 yrs.; swelling on left side | Mesenterial cyst | Reduction | Treitz | Recovery | ..... |
| Gibby, 1928..... | | M | 37 | Sausage-like mass on left side for 2 yrs.; pain for 2 wks. | Probable retro-peritoneal sarcoma | Reduction | Intersigmoid | Recovery | Roentgenogram showed obstruction |
| Godard and Smith, 1929 | | .. | .. | Subacute gastric symptoms | Duodenal stasis | (1) Gastro-enterostomy; (2) reduction | Transverse mesocolon | Recovery | Roentgenogram showed duodenal stasis; hernia not diagnosed first operation |
| Green, 1927..... | | M | 42 | Occasional gastric disturbance; pain in abdomen; vomiting; constipation | Not made | Enterotomy reduction | Foramen of Winslow | Death | ..... |
| Hamilton, 1926..... | | .. | .. | Colicky pain; vomiting for 6 wks. | Intestinal obstruction | Reduction | Intersigmoid | Death | Death due to aneurysm on 19th day |
| Heaney and Simpson 1925 | (*a*) | F | 52 | Chronic gastric symptoms; occasional vomiting; 12 mos. previously acute pain in stomach | Tumor | Gastro-enterostomy | Transverse mesocolon | Recovery | Hour-glass stomach |
| | (*b*) | F | 38 | Gastric disturbance for 16 yrs.; gastric hemorrhage 18 mos. ago; vomiting; pain for 6 wks. | | Reduction; stomach resected | Transverse mesocolon | Recovery | Roentgenogram showed hour-glass stomach |
| Hennig, 1926..... | | F | 16 | Chronic abdominal pain; acute for 24 hrs. | Ovarian tumor | End-to-end anastomosis | Retrocolic | Recovery | ..... |
| Jackson, 1930..... | | .. | .. | Digestive disturbances | Hernia | Reduction | Foramen of Winslow | Recovery | Diagnosis by roentgenogram |
| Janes, 1929..... | (*a*) | F | 58 | Repeated attacks of abdominal pain for 10 mos.; last attack of pain with distention | Cyst | Reduction | Left broad ligament | Recovery | ..... |
| | (*b*) | F | 36 | Abdominal pain, cramps, vomiting; one previous attack | Not made | Exploratory | Left broad ligament | Death | Death due to cardiac failure; autopsy showed hernia |
| Judd, 1929..... | | M | 10 | Abdominal pain, vomiting for 3 days | Obstruction | Reduction | Through mesentery | Recovery | ..... |
| Koch, 1926..... | | F | 15 | Severe abdominal pain for 3 days | Ovarian cyst | Reduction | Transverse mesocolon | Recovery | ..... |
| Kostić, 1927..... | | M | 33 | Colicky pains, vomiting; onset sudden | Intestinal obstruction | Reduction | Intersigmoid | Recovery | ..... |

TABLE 4.—*Cases of Internal Hernia Reported Since 1925—Continued*

| Author | | Sex | Age | Symptoms | Preoperative Diagnosis | Operation | Type of Hernia | Results | Comment |
|---|---|---|---|---|---|---|---|---|---|
| Lefèvre, 1927 | | M | 44 | Symptoms typical pyloric stenosis; chronic gastric symptoms | Pyloric stenosis | Gastro-enterostomy | Transverse mesocolon (congenital) | Recovery | Diagnosis by roentgenogram |
| Liebers, 1926 | | .. | .. | ..... | ..... | ..... | Treitz | Death | Died of miliary tuberculosis; hernia at autopsy |
| Long, 1929 | (*a*) | M | 51 | Cramp-like pains, vomiting | Obstruction | Reduction | Retro-peritoneal | Recovery | ..... |
| | (*b*) | M | 24 | Abdominal pain, colic, nausea | Not given | Reduction | Retrocolic | Recovery | ..... |
| Lower and Higgins, 1925 | (*a*) | F | 13 | Abdominal distention, vomiting for 9 wks. | Intestinal obstruction | Reduction | Right para-duodenal | Recovery | ..... |
| | (*b*) | M | 50 | Abdominal distention, pain, nausea, constipation; mass in region of cecum for 2 yrs. | Tumor of cecum | Reduction impossible | Left para-duodenal | Recovery | ..... |
| Malcomb, 1927 | (*a*) | M | 22 | Sudden pain, vomiting, prostration | Intestinal obstruction | Reduction | Duodeno-jejunal | Recovery | ..... |
| | (*b*) | M | 18 | Sudden abdominal pain, vomiting; similar attack 3 yrs. ago | Acute appendicitis | Reduction | Ileo-appendicular | Recovery | ..... |
| Martzloff, 1930 | | F | 24 | Gas, epigastric fulness several years; acute discomfort, nausea, vomiting for 7 days | Pyelitis; possible appendicitis | Reduction | Through omentum | Recovery | ..... |
| Masson, 1930 | | .. | .. | Epigastric pain for 12 yrs.; bloating, vomiting | Probable cholecystitis; obstruction | Reduction; resection ileum | Right para-duodenal | Recovery | ..... |
| McCarthy, 1926 | | M | 20 | Extreme shock; severe abdominal pain; nausea, marked tenesmus; sudden onset | Ruptured appendix; perforated intestinal ulcer | Resection impossible; all small; part large bowel gangrenous | Intersigmoid | Death | Diagnosis not made until 18 hours after onset |
| Muller, 1928 | | M | 39 | Sudden abdominal pain; vague symptoms for 10 to 15 yrs.; constipation alternated with diarrhea | Gangrenous appendix | None | Through mesentery | Death | Died before operation was possible |
| Nel, 1929 | | F | .. | Acute abdominal pain; vomiting; collapse | Perforated gastric ulcer | Reduction | Through transverse mesocolon | Recovery | Possible cause—fall from horse |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Odermatt, 1926 | | F | 68 | Abdominal distress for 3 yrs.; loss of weight; vomiting | Intestinal cancer | None | Through transverse mesocolon | Death | Condition too bad for operation |
| Siegmund, 1927 | (a) | M | 18 | ..... | ..... | None | Under mesocolon | Death | Autopsy, died of grip |
| | (b) | F | 32 | ..... | ..... | None | Under mesocolon | Death | Autopsy, died of angioma |
| | (c) | M | 74 | Symptoms intestinal obstruction for 20 yrs. | ..... | None | In meso-sigmoid | Death | Autopsy, died of appendicitis |
| Stangl, 1930 | | .. | .. | No symptoms of obstruction | Bullet wound | None | Para-duodenal | Death | Hernia at autopsy |
| Steinke, 1931 | (a) | M | 43 | Acute abdominal pain; shock; vomiting; pancreatic symptoms; abdominal pain for 4 yrs. | Intestinal obstruction; pancreatitis | Reduction | Left para-duodenal | Recovery | ..... |
| | (b) | F | 29 | Bloating gas; severe abdominal cramps; vomiting for 2 days | Abdominal tumor | Peritoneal holes sutured | Left para-duodenal | Recovery | ..... |
| | (c) | M | 26 | Pain, colic for 2 wks. | Obstruction | Reduction | Transverse mesocolon | Recovery | Subsequent to posterior gastro-enterostomy |
| Sumner, 1929 | | M | 66 | Abdominal symptoms for years; symptoms obstruction | Intestinal obstruction | Reduction | Retro-peritoneal | Death | Autopsy, pneumonia |
| Thevenard, 1928 | | M | 59 | Operation for rectal neoplasm 3 mos. previously; sudden epigastric pain, fecal vomiting | Not given | Reduction | Foramen of Winslow | Death | Operation 5 days after onset |
| Traum, 1931 | | M | 64 | Acute pain in hypogastrium; vomiting | Acute appendicitis | Reduction | Ileo-appendicular | Recovery | ..... |
| Turner and Scholefield, 1930 | | .. | .. | Acute abdominal pain, vomiting subsequent to operation for perforated ulcer | Intestinal obstruction | Two loops intestine punctured | Left para-duodenal | Death | ..... |
| Venables, 1930 | | M | .. | Chronic intestinal flatulence; diarrhea for 3 wks.; pain for 3 days | Partial obstruction | Reduction | Right para-duodenal | Recovery | Roentgenogram showed obstruction |
| Vidgoff and Sturgeon, 1930 | | .. | .. | Severe generalized abdominal pain; vomiting for 5 hrs. | Acute appendicitis or obstruction | Reduction | Retrocolic | Recovery | ..... |
| Watschugoff, 1931 | (a) | M | 24 | Sudden pain, nausea | "Ileus" | Reduction | Fovea supravesicalis | Recovery | ..... |
| | (b) | M | 50 | Pain for 4 days, vomiting | "Ileus" | Reduction | Fovea supravesicalis | Recovery | ..... |
| | (c) | M | 29 | Sudden abdominal pain | Obstruction | Reduction | Fovea supravesicalis | Recovery | ..... |

Janes, who reported two cases of hernia through an opening of the left broad ligament, felt that these lesions can hardly be diagnosed before operation.

Donald reported a case of strangulated hernia in the retro-appendicular paracecal pouch. He was of the opinion that the pouch was caused by a lack of fusion between the mesocolon and the posterior parietal peritoneum in the terminal stage of embryonic rotation of the intestine. He said that he could find no previous description of this fossa and that neither Moynihan nor Short mentioned it.

TABLE 5.—*Comparison of Short's Figures with Those Reported by Other Authors*

| | Operation | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Death | | | | Died—No Operation | | | |
| | Recovery | | Short | | Others | | Short | | Others | |
| Type of Hernia | Short | Others | | Per Cent | | Per Cent | | Per Cent | | Per Cent |
| Retroperitoneal | .. | 1 | .. | .... | 1 | 50.0 | .. | .... | .. | .... |
| Paraduodenal | | | | | | | | | | |
| Side not given | .. | .. | .. | .... | .. | .... | .. | .... | .. | .... |
| Left | 27 | 4 | 16 | 37.2 | 1 | 33.3 | .. | .... | .. | .... |
| Right | 1 | 4 | 1 | 20.0 | .. | .... | 3 | 60.0 | .. | .... |
| Duodenojejunal | .. | 4 | .. | .... | .. | .... | .. | .... | .. | .... |
| Treitz | .. | 2 | .. | .... | 2 | 40.0 | .. | .... | 1 | 20.0 |
| Paracecal | | | | | | | | | | |
| Retrocolic | 12 | 4 | 4 | 23.5 | .. | .... | 1 | 5.8 | .. | .... |
| Ileo-appendicular | 2 | 3 | 1 | 20.0 | 1 | 25.0 | 2 | 40.0 | .. | .... |
| Foramen of Winslow | 8 | 6 | 11 | 45.8 | 4 | 40.0 | 6 | 25.0 | .. | .... |
| Intersigmoid | 4 | 2 | 2 | 25.0 | 2 | 50.0 | 2 | 50.0 | .. | .... |
| Transverse mesocolon | 6 | 7 | .. | .... | .. | .... | .. | .... | 1 | 12.0 |
| Others | 9 | 8 | .. | .... | 3 | 27.2 | 1 | 10.0 | 1 | 9.0 |
| | 69 | 45* | 35 | 29.6 | 14† | 21.3 | 15 | 12.7 | 3 | 42.3 |

Total number of cases: Short, 118 cases, 50 deaths; mortality 42.3 per cent.
Total number of cases: Others, 61 cases, 17 deaths; mortality 27.8 per cent.
* Including two cases through the foramen of Winslow and one duodenojejunal hernia not quoted by Short.
† Including one case through the foramen of Winslow, one ileocecal and one through the omentum missed by Short.

The three cases reported by Watschugoff of intra-abdominal hernias of the fovea supravesicalis have been included here. They are definitely designated as of the internal type. Watson said that this type of hernia may be either external or internal. Watschugoff reported that in the past ten years in the Rasumowsky Clinic there were fifteen hundred operations for hernia, but only three of this type. He stated that sixteen similar cases have been reported by Reich.

Martzloff reported a case of prolapse of the intestine through a preformed opening in the great omentum. On inspection, two openings in the omentum in about the midline, a smaller and a larger one, were found. A loop of small intestine protruded through the larger defect and lay on the omentum to the right of the midline. His case differs from others in the literature in not having symptoms of intes-

tinal obstruction. There are, he said, sixteen such cases reported in the literature in which the opening in the omentum was preformed, and not the result of adhesions.

Four cases of intersigmoid hernia are reported here, in two of which the patient died following operation. Hamilton, who contributes one of the latter cases, said that Short had overlooked at least six cases. His own case, he stated, brings the total up to fifteen. The three additional cases collected here all occurred in males, which supports his statement that of the fifteen reported up to that time only two occurred in females. The youngest patient whose case has been reported was an infant 3½ days old (reported by Coley). The oldest patient was a man of 66 years.

Deaver (*a*), reporting a case of paraduodenal hernia, said that this condition is usually only discovered at autopsy. Of the twenty-nine cases which he quoted Nagel as reporting in 1923, operation was performed in twelve and ten were fatal. This would give a mortality of 83 per cent. Short reported five cases with one death following operation and three deaths without operation, a mortality of 80 per cent. Of the four cases of right duodenal hernia collected in this paper, recovery followed operation in all of them. Masson asserted that in no case has diagnosis been made before operation or autopsy. The case he reported resulted in recovery.

Turner and Scholefield, reporting a case they classed as duodenal retroperitoneal hernia, said that this is a very rare occurrence; that in Guy's clinical and postmortem reports from 1900 to 1925 there is only the one case.

Godard and Smith, writing of hernias of the retroperitoneal cavity, reported that Federschmidt has collected thirty-one cases of hernias through the transverse mesocolon and an additional fifty-two cases of internal hernia through the mesentery orifice. They consider that accidents to the mesentery are very rare, and that inflammation and neoplasm play a rôle no less important than traumatism. They mention the relatively high number of gastric or duodenal ulcers or carcinomas that exist with a hernia through the mesotransverse colon. Lombard, they said, reported carcinoma or ulcer eighteen times in twenty-eight cases. Cases are known in which such hernias are congenital. Pringle, in 1919, reporting eight cases, had one in a girl of 5 years and another in a boy of 5 months. The girl had a mesotransverse colon which was incompletely developed, and a large part of the jejunum had penetrated into the retrogastric pocket. Death resulted. The boy also died. Autopsy showed a very large space between the left and middle colic artery which was closed by a mesentery fringe. The hernias through the transverse mesocolon are considered by Godard

and Smith to be the most favorable of the internal hernias, though they frequently follow gastro-enterostomy.

Watson said that hernias through the transverse mesocolon are rare; that in sixteen hundred autopsies reported by Mitchell, in only three were there holes in the mesentery, and in no cases were hernias found. Heaney and Simpson reported that in twenty-one cases of this type, gastric or duodenal ulcer or carcinoma was present in fourteen, a finding in agreement with the belief of Godard and Smith. In fourteen cases in which sex was mentioned, thirteen of the patients were females. Heaney and Simpson consider a midline ptosis, which predisposes to ulcer and hour-glass stomach, an all important factor in the production of this type of hernia. It was definitely present in ten of twenty-one cases, and both of their cases showed it. Lefèvre also noted the frequent coexistence of gastric or duodenal ulcerous lesions and internal hernias, but said that cause and effect cannot be concluded from this. In his case he believed the orifice to be of a congenital nature.

Short reported seventeen cases of hernias through the transverse mesocolon, in six of which recovery followed operation. The fate in the other eleven is not given in his tabulation. In the eight cases reported since 1925, there was one death in a case in which operation was not performed.

Short collected twenty-four cases of hernia through the foramen of Winslow. In this paper are reported four additional cases which Short missed and seven cases which have been reported since his paper was written, bringing the number up to thirty-five. Short found a mortality of 70.8 per cent for this type of hernia, but the figures reported since then are lower, the mortality being 42.7 per cent. Deaver (*a*) said that this type of hernia presents a very difficult problem because of the danger incident to injuring the neck of the hernia, which has within its immediate vicinity the portal vein, the hepatic artery, the common bile duct, the inferior vena cava and the first portion of the duodenum. Jejunostomy is usually the only safe procedure. Dewis and Miller said that this type of hernia gives symptoms of epigastric discomfort, weight, swelling, fulness and pressure. There is absence of definite obstruction. With this conclusion, the cases reported here are in agreement. Gastric symptoms, often of long duration, predominate. In the case reported by Aigrot, there was a history of stomach trouble extending over twenty years.

Godard and Smith also spoke of the difficulties of reducing hernias through the foramen of Winslow. They report that often the difficulties are insurmountable.

Short reported seventeen cases of retrocolic hernia. To this list there have been added four more. Short's mortality is 29.4 per cent.

In the four cases reported in this paper recovery followed operation. The case of Vidgoff and Sturgeon is remarkable because the hernia involved the cecum, which formed part of the contents of the fossa. The authors said that this is the only case on record in which this has occurred.

As has been mentioned, hernia of Treitz is a term that Short does not use. In this paper six cases have been so classed by their authors. In addition, there were two cases that Garber quoted and that are listed in tables 1 and 2. In two of the six cases, operation was not performed, and the hernia was discovered at autopsy. In the remaining four death occurred in two following operation. In one of these cases the hernia was only discovered at autopsy. Short said that ninety cases are known, the patients ranging in age from 2 months to 80 years; that the male sex predominates, and generally it is believed there is an embryonal disposition and that the hernia develops as the result of a mechanical factor on a disposition already present. Garber listed the usual symptoms of this type of hernia as follows: (1) dyspeptic symptoms; (2) sensation of tumor in the abdomen, localized and periodically changing in size; (3) periodic swelling of the abdomen, and (4) tympanic sound over the abdomen. Christophe expressed the belief that duodenojejunostomy is the operation of choice in this type of hernia when reduction is impossible.

Spitzmuller reported a case of double hernia (colonic rectal ileus and internal rectovaginal) which, because of its complex nature, has not been included in the tables. The left scrotal hernia was evident, but operation revealed the double hernia. Reduction of the hernia resulted in recovery.

### MORTALITY FIGURES

In looking over table 4 it will be seen that of the sixty cases operation was performed in fifty-two; eleven of the patients died and forty-one recovered. Of the nineteen deaths, five were due to causes other than hernia, and the hernia was discovered only at autopsy. Thus in Lieber's case death was due to tuberculosis; in Stangl's case death was due to accident; and in the three cases of Siegmund death was due, respectively, to grip, angioma and appendicitis. Three of the remaining fourteen patients who died were seen in the terminal stage when operation was no longer possible. These were the cases of Odermatt, Debray and Muller. Of the eleven cases in which operation was done and in which death ensued, delay before operation or the fact that the hernia was undiagnosed even at operation played a major part in the cause of death. McCarthy's patient was already in shock when seen, and it was not until eighteen hours after the onset of the condition that the operation was done. Delay undoubtedly contributed to death

in Thevenard's case. The first physician to see the man ordered a purgative, and the patient was not brought in for operation until five days after the onset of the symptoms. In James' second case an exploratory operation was done in spite of a bad cardiac condition, and death followed from myocardial failure. It was only at autopsy that the cause of the abdominal symptoms was found to be hernia.

Christophe reported a case of hernia of Treitz which illustrates perfectly the difficulty in diagnosing this condition, as well as the dangers attendant on a late diagnosis. His patient, who had suffered from dyspeptic troubles for five years, and for two years with alternative diarrhea and constipation, suddenly, six weeks before, had abdominal pain and noted a tumor. A preoperative diagnosis could not be made, and roentgenograms revealed no obstruction. An exploratory operation was performed, and what was supposed to be a retroperitoneal ganglionary tumor was found. The wound was closed. There was temporary amelioration following the operation, then the condition became worse, the roentgenogram showed a dilated duodenum, and a resistent mass was felt in the left hypochrondriac region. Duodenojejunostomy was refused until the condition was very bad. The operation was performed, and a hernia was found and reduced. Death followed from a laryngitis not severe in itself, but fatal because of the extreme cachetic condition.

In Christophe's second case, in which death followed a celiotomy, symptoms of intestinal obstruction had been present for a week. Dewis and Miller reported a case in which, at operation, they found and drained what they thought to be a tumor. At autopsy the true condition, a hernia, was disclosed. Donald's patient with symptoms of acute obstruction beginning four days before the operation died two hours after being operated on.

In a few instances death was not directly due to the hernial condition. Thus Sumner's patient died of pneumonia, and Hamilton's patient of aneurysm on the nineteenth postoperative day.

These figures show without doubt that delay in operation is far too often the cause of fatality.

Diagnosis is exceedingly difficult before operation and, as has been mentioned, in more than one case the true condition is not discovered at operation. In many cases the immediate symptoms are those of intestinal obstruction, as would be expected, since incarceration or strangulation of the hernia is common. In addition to the preoperative diagnosis of obstruction, the diagnoses of perforated ulcer and of appendicitis are both common. When palpation reveals a mass, the diagnosis may be cyst or malignancy. The only instances in which a hernia was suspected before operation were the cases of Erdély, Jackson, and Coley and Hoguet. In Jackson's case the diagnosis was made

by roentgenogram. In the case of Coley and Hoguet the mass was palpated, but the physicians called in consultation were unable to confirm this finding before operation. Gastric symptoms are frequently of long duration, and in many instances there are recurring attacks of pain and vomiting. These are frequent enough to be considered characteristic.

The mortality in the reports in the literature since Short's article is much less than that given by Short. These are given in detail in table 5, and compared there with those of Short. In the sixty-one cases here reported with hernia in which operation was performed, or in which death occurred without operation as a direct result of the hernia, there were seventeen deaths, or 27.8 per cent. This compares favorably with Short's figure of 42.3 per cent. In the cases in which operation was performed Short reported a mortality of 29.6 per cent, while the mortality in the cases reported here in which operation was performed is only 21.3 per cent.

### SEX AND AGE

Internal hernia is more common in males than in females. From the cases here reported the ratio is better than 2:1, there being thirty-six cases in males and only fifteen in females. The youngest patient, a 10 year old boy, had a hernia through the mesentery (case reported by Judd). The oldest patient was a man of 74 who died of appendicitis without operation (case reported by Siegmund). The average age is 38, but there are only six cases in the forty-eight in which the age is stated in which the patient is less than 20. There are fifteen patients, or almost one-third, who are 50 or over.

### TYPE OF OPERATION

The difficulties of diagnosis have already been noted. The symptoms, while not sufficiently differentiated from other gastric and abdominal complaints, are usually sufficiently severe, especially when strangulation is present, to warrant immediate operation. The type of operation depends largely on the condition of the bowel. In many instances simple traction will be sufficient to reduce the hernia, and often the release of the obstruction will be sufficient to restore normal blood flow and color, making more radical procedure unnecessary. When adhesions are present they must, of course, be cut away. Occasionally the pouch incarcerating the bowel needs to be divided. When necessary, jejunostomy, end-to-end anastomosis and other radical procedures must be performed. A glance at table 4 will show that where such procedures have been necessary the mortality has been greatly increased.

### CAUSES

Some mention has been made already of the various opinions as to the cause of internal hernia. Little can be added. Trauma, congenital defects, previous operations, ulcers and malignancy all have played their part. In most instances the direct cause of the condition cannot be discovered, and speculation is idle.

### SUMMARY

1. A review of the literature of internal hernia since Short's article has been made and the cases collected.

2. A systematic classification of internal hernia is given.

3. Tables showing the mortality, frequency of the various types and a list of the collected cases are given.

4. Three new cases are reported.

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# RADIOSENSITIVENESS OF CELLS AND TISSUES, AND SOME MEDICAL IMPLICATIONS

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Casual reading of contemporary medical records bearing on the action of roentgen rays and radium often gives the impression that little is known of such action in spite of the fact that substantial or conclusive experimental data are available to indicate or to establish clearly the nature of it. In some cases, indeed, the experimental indications are absolute. In other cases, the experimental evidence may be inadequate, but the clinical data may be sufficient to suggest the probable effect of irradiation. It is true that many problems relating to radiotherapy are still the subject of controversy, and that the large number of experiments that have been made have yielded only partial answers to many questions. Nevertheless, the facts already brought to light are sufficiently numerous to provide an imposing, although admittedly incomplete, scientific background. Unfortunately, the evidence furnished by experiments on animals and clinical observation has never been analyzed and correlated, and much of it has been lying on library shelves, buried in medical or other journals that are seldom read. Even among medical radiologists knowledge of the experimental background is not widely diffused.

The law based on the extensive investigations of Bergonié and Tribondeau (1904-1907), according to which young or immature cells are more radiosensitive than old or adult cells, has been generally recognized and has long been regarded as the essential foundation of radiotherapy. Numerous experiments have shown that direct irradiation of the pregnant uterus or of the young soon after birth causes retardation of growth of the skeleton and of various organs, including the brain. The degree of such effect varies with the dose, the age of the animal and the natural life cycle of the species. The cells and tissues of a given species rapidly become less sensitive as the animal emerges from the early phase of its existence, during which growth is a prominent feature. Indubitable as is the relation of the age of cells to radiosensitiveness, analysis of the experiments made to test the susceptibility of different organs and tissues brings out the even more important fact that each

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variety of cell in the body has a specific sensitiveness, or rather a specific range of sensitiveness, to irradiation. This is not intended to imply that all cells of one kind, such as lymphocytes or squamous epithelial cells, react in precisely the same way to a given dose of rays. A certain measure of variation in reaction must occur, because different cells of the same kind are struck by the rays while in different stages of metabolism. Other still unknown factors also may play a part. However, if allowance is made for such variation, and if reaction time is taken as a criterion, the specific sensitiveness of each kind of cell looms up as the dominant single fact of radiology and deserves to be recognized as a law. And yet, if one may judge by present day writings, the existence of such a law and of its medical and biological implications is not at all realized. For years much has been made of the dogma that pathologic cells are more radiosensitive than normal cells of the same kind, but, as Lazarus-Barlow and others have shown, the foundation on which this dogma rests is tenuous and insecure. The physiologic condition of cells undoubtedly has some influence on their sensitiveness, but, as I shall bring out presently, this influence is small as compared with the specific natural susceptibility of each variety of cell. Although the factors responsible for such specificity have not yet been determined, the sensitiveness peculiar to each kind of cell appears to be related chiefly to the natural life cycle. Thus the lymphocytes, the metabolic cycle of which among human cells is the shortest, are also the most radiosensitive, and the nerve cells, the life cycle of which is the longest, are also the most resistant to irradiation. But to this question as to many others the final answer has not yet been given.

When a living tissue or organ is exposed to roentgen rays or radium, a more or less important proportion of the cells may subsequently exhibit temporary inhibition of metabolic activity or complete and permanent disintegration, or may not show any deleterious effect. Moreover, if the time intervening between irradiation and perceptible reaction is taken as a criterion, it will be found that certain species of cells react more rapidly than others to a given dose, or that the degree of reaction to the same dose is greater for some kinds of cells than for others. According to present knowledge, cells may be classified, according to their radiosensitiveness, in the following order:

Lymphoid cells (lymphocytes)

Polymorphonuclear and eosinophilic leukocytes

Epithelial cells: (1) basal epithelium of certain secretory glands, especially of the salivary glands; (2) basal epithelium (spermatogonial cells) of the testis and follicular epithelium of the ovary; (3) basal epithelium of the skin, mucous membranes and certain organs, such as the stomach and small intestine; (4) alveolar epithelium of the lungs and epithelium of the bile ducts (liver), and (5) epithelium of tubules of the kidneys

Endothelial cells of blood vessels, pleura and peritoneum

Connective tissue cells
Muscle cells
Bone cells
Nerve cells

Although the difference in susceptibility between the most sensitive and the least sensitive varieties of cells is considerable, none of the cells are wholly invulnerable to irradiation; all cells, whatever their variety, may be destroyed or injured if exposed to a sufficiently large dose of rays, especially if doses within the therapeutic range are disregarded.

### RADIOSENSITIVENESS OF DIFFERENT SPECIES OF CELLS

*Lymphoid Cells.*—Of the different kinds of cells that make up the tissues and organs of the body, the most susceptible by far are the lymphocytes. This important fact was brought to light by the early and extensive experiments of Heineke (1903, 1904, 1905) and has since been fully confirmed by the subsequent investigations of Warthin (1906), Krause and Ziegler (1906-1907), Fromme (1917), Hartmann (1920), Jolly (1924), Tsuzuki (1926), Piepenborn (1929) and others. When, using different species of animals, Heineke exposed the entire body to roentgen rays, he found that most of the tissues and organs remained unaffected, but that the spleen, lymph nodes, intestinal lymph follicles, circulating blood, bone marrow and all agglomerations of lymphoid cells showed a more or less pronounced destruction of lymphocytes. The degree of destruction was proportional to the dose of rays and varied with the interval between irradiation and death. In the spleen, lymph nodes and other lymphoid structures, the destruction of lymphocytes started around the germinal center and gradually extended toward the periphery of the follicle. As the number of intact lymphocytes diminished, the stroma became prominent, and often this feature was so pronounced that the follicles could be recognized only by the blood vessels and the concentric arrangement of the stroma. Heineke observed such destruction of lymphocytes as early as two hours after irradiation. The extent and duration of the destructive phase depended on the intensity of irradiation; the destruction continued for several days and was accompanied by a progressive reduction in volume, or atrophy, of the affected structures.

As described by Heineke, such destruction is characterized by disorganization and fragmentation of the nuclear chromatin and by scattering of the fragments of chromatin between the remaining intact cells and in the reticular spaces, where the fragments gather into clumps or balls. Then the clumps or balls of degenerate chromatin are gradually taken up by some of the reticular cells, which assume a phagocytic property and swell as the amount of ingested chromatin débris increases. The disposal of chromatin material from the destroyed

cells continues until all such material has undergone phagocytosis. The nuclear débris ingested by the phagocytes apparently undergoes intracellular digestion, because the number and the size of the ingested fragments diminish steadily. Some hours later the phagocytic reticular cells themselves begin to disappear. After a single massive irradiation or repeated moderate doses, all the lymphocytes may be destroyed, but after a single small or moderate dose a certain proportion of the cells appear to resist the action of the rays. From one to three weeks after exposure, if the irradiation has not been sufficiently intense to destroy all the lymphocytes, more or less regeneration of the lymphoid tissue may be observed, and complete cellular restoration may occur. Two or three days after exposure to roentgen rays, degenerative alteration of other cells, notably the polymorphonuclear and eosinophilic leukocytes, also becomes perceptible, and many of these cells disappear from the splenic pulp and bone marrow.

Warthin's description of the effect of roentgen rays on the lymphoid structures corroborates the observations of Heineke in every particular, except that, by examining the tissues soon after irradiation, Warthin found unmistakable evidence of the disintegration of lymphocytes within fifteen minutes after exposure of the animals to the rays, and the cellular degeneration continued for several days. Similar effects were obtained with radium by London (1903), Heineke (1904), London (1905), Thies (1905) and Lazarus-Barlow (1922). Rudberg (1907), Aubertin and Bordet (1909), Arella (1910), Regaud and Crémieu (1912) and others have likewise shown that roentgen rays and radium exert precisely the same influence on the small round cells of the thymus gland, and their work strongly supports Hammar's conclusion that the small cells of the thymus gland are indeed lymphocytes. Others, notably Senn (1903), Heineke (1903, 1905), Guilloz and Spillmann (1904), Aubertin and Beaujard (1904, 1905, 1908), Brown (1904), Bryant and Crane (1904), Capps and Smith (1904), Helber and Linser (1905), Benjamin, von Reuss, Sluka and Schwarz (1906), Aubertin and Delamarre (1908), Taylor, Witherbee and Murphy (1919), Russ (1919, 1921) and Leitch (1921), have proved conclusively that the lymphocytes in the circulating blood are equally sensitive to irradiation and also are destroyed in large numbers by exposure to roentgen rays or radium.

*Epithelium of the Salivary Glands.*—Next to the lymphocytes in point of radiosensitiveness are the basal epithelial cells of the salivary glands. Actually these cells are more sensitive to irradiation than the polymorphonuclear and eosinophilic leukocytes. This is evidenced by the fact that, whereas microscopically perceptible changes in the two latter varieties of cells can seldom be found within the first six hours after exposure to the rays, clinical signs of salivary reaction can

usually be observed in from three to six hours after irradiation. These signs consist in swelling, redness and tenderness in the region of the irradiated glands and, when bilateral, may simulate the salivary phase of mumps. If all the glands on both sides have been exposed to the rays, the foregoing clinical signs may be rapidly followed by decrease in salivary secretion, often leading to dryness of the mouth lasting from a few days to two or more weeks. This reaction of the salivary glands is characterized by mucoid degeneration of the basal epithelium. The cells swell, the excretory ducts become occluded, and the secretion accumulates within the glands—hence swelling and tenderness of the glands and dryness of the mouth. Following a single irradiation, salivary reaction is always transient; after a time, usually from twenty-four to seventy-two hours, the acute phase of the reaction subsides, and the clinical signs gradually abate. Following repeated irradiation, however, the secretory function of the glands may cease, and dryness of the mouth may persist for a long time. Such effects occur only when the glands on both sides have been exposed to the direct action of the rays. Salivary reaction does not occur when other parts of the body are irradiated, and exposure of the glands on one side causes a reaction on that side only. When the reaction is unilateral, dryness of the mouth is seldom noticed, undoubtedly because the glands on the opposite side furnish a sufficient quantity of saliva to lubricate the oral mucosa. The experiments of Lazarus-Barlow (1922) and of Mottram (1923) indicate that epithelial cells that produce mucus are much more sensitive to irradiation than other epithelial cells. The first effect is mucoid degeneration with excessive and abnormal production of mucus, followed by arrest of the formation of mucus. This has been shown to occur in the intestine, and the behavior of the salivary glands under irradiation makes it seem likely that the mucus-producing cells in the epithelial lining of these glands are similarly affected by the rays.

*Epithelium of the Testis and Ovary.*—The testis is not so sensitive as some of the leukocytes or as the salivary glands, but with the exception of these, is the most sensitive structure in the body. This susceptibility has been established by numerous experiments on animals, as well as by the cessation of seminal function in radiologists and other persons exposed to roentgen rays over a long period of time. The radiosensitiveness of the organ is due to the susceptibility of the spermatogonial cells, which are affected deleteriously even by a moderate dose of roentgen rays. The cells of Sertoli are relatively resistant to irradiation, and this fact tends to support the view that they supply nourishment to the basal layer of seminal cells, the spermatogonia. The spermatocytes of the first and second order, as well as the spermatids and mature spermatozoa, are distinctly less sensitive than the spermatogonia and are affected only by larger doses. Even so, much of the

cellular degeneration is probably secondary to the direct action of the rays on the basal cells. Microscopic examination of the seminal tubules several days after irradiation may disclose vacuolization and degeneration of some or all of the spermatogonia, depending on the dose of roentgen rays to which the organ has been exposed. After a sufficiently large dose, degeneration of the spermatogonia proceeds to complete disintegration. This is accompanied by failure of the cells to evolve into spermatocytes and mature spermatozoa, and the final result is permanent azoospermia. After a dose insufficient to cause permanent azoospermia, a certain proportion of the spermatogonia may be able to survive and may serve as a nucleus for histologic regeneration and functional restoration. Large doses repeated at comparatively short intervals are almost certain to induce permanent sterilization. The interstitial tissue, on the other hand, is much more resistant and is not perceptibly influenced by ordinary therapeutic irradiation. Needless to say, however, that even the interstitial tissue could be irreparably injured by excessive irradiation beyond the therapeutic range.

The radiosensitiveness of the ovary is essentially the same as that of the testis, and the cells to which the specific susceptibility of the gland is due are the ova and the epithelium of the follicles. The sensitiveness of different follicles varies according to the stage of development. Depending on the dose of rays to which the ovary has been exposed or on the number of times a given dose has been repeated, the effect of irradiation may be disintegration and disappearance of a certain proportion of the follicles or complete and permanent destruction of every follicular structure. A certain proportion of the primordial follicles may escape if the dose has been small. Moreover, the steps in the reaction of the follicles are analogous to those of spontaneous physiologic atresia. Follicular reaction appears from three to six hours after exposure and is particularly marked in the mature follicles. In the primordial follicles, the rays act on the ovum sooner than on the follicular epithelium, and this action is featured by pyknosis of the germinal vesicles, condensation of the protoplasm and finally by chromatolysis and fragmentation of the cell. The cellular fragments then undergo phagocytosis by the follicular epithelial cells, which themselves degenerate as soon as phagocytic disposal of the fragmented ova is complete. These different steps require three or four days, but since all the follicles do not begin to react at the same time, a week or more may elapse before all the affected follicles have disappeared. The same cycle of changes occurs in the more mature follicles with several layers of epithelium, but in these the follicular epithelium is more sensitive, and its cells undergo rapid autolysis. Moreover, the connective tissue cells of the theca interna degenerate as rapidly as the epithelial cells. In the still more mature follicles, in which the ovum

is large and separated from the follicular epithelium by a membrana pellucida, the epithelial cells first penetrate this membrane by diapedesis, dispose of the degenerated ova by phagocytosis, and in turn degenerate and disappear. Migration of the epithelial cells begins about the third day, and the degenerative process continues for two or three weeks. All such follicles may be destroyed by irradiation, but on account of the large size of the ova the autolytic process may require considerable time. In fully developed follicles, the epithelial cells are still more sensitive, most of the parietal epithelium of the follicular cavity being destroyed by irradiation, whereas the epithelial cells that surround the ovum are slightly less sensitive. Sometimes irradiation may be followed by an accelerated maturation of the ovum followed by degeneration. Thus the radiosensitiveness of ovarian follicles increases in proportion to their development. The interstitial cells of the ovary do not appear to be influenced directly by the rays, but slowly disappear, probably because the destruction and disappearance of the follicles prevent the interstitial cells from being renewed.

*Epithelium of the Skin, Mucous Membranes and Gastro-Intestinal Tract.*—The skin can tolerate with impunity a considerable single dose of roentgen rays, but when the limit of tolerance is exceeded, it may undergo a series of reactive changes. The first clinical manifestation of excessive irradiation is a readiness of the hair in the exposed territory to fall out. After a still larger dose not only does epilation occur, but varying degrees of reactive inflammation of the skin may take place. Dermatitis may appear as a slight erythema lasting a few days and followed by pigmentation corresponding to the exposed area; as a more pronounced, bright red erythema with a sensation of heat, followed by the formation of vesicles and later by itching, exfoliation of the epidermis and deep pigmentation; or, in extreme cases, as an intense, painful erythema, with or without fever, and followed by more or less extensive ulceration of the entire thickness of the skin. Mild radiodermatitis may not leave any permanent marks beyond slight atrophy of the irradiated area of skin, provided the inflammatory reaction results from a single exposure. When such reaction appears after the same area of skin has been exposed several times, it is likely to be followed, from one to three years later, by telangiectasis. The sudoriferous and sebaceous glands of the irradiated skin also undergo degenerative changes. Radiodermatitis accompanied by the formation of vesicles is followed by more extensive desquamation or by the actual formation of small rounded, or large irregular cutaneous scars. When severe radiodermatitis is followed by ulceration, the ulcers are slow to heal. This is due partly to the peculiar character of injury produced by irradiation and partly to secondary infection, which so commonly complicates the ulceration. Severe radiodermatitis generally

results from inexperience, from miscalculation of some of the factors in dosage, or from accidental omission of a filter with a dose based on the use of filtered rays.

The rays act first on the epithelium of the hair follicles, and this explains the loosening or falling of the hair. Such elective sensitiveness of the hair follicles is made use of in the treatment of diseases of the skin such as ringworm, in which the dose of roentgen rays is adjusted so as to cause temporary epilation. The success of the treatment rests on the ability of the radiologist to regulate the dose within narrow limits; any uncertainty in this respect may result in permanent alopecia or worse. When the dose has been sufficient to cause distinct erythema, the microscopic changes include irritative disturbance of the basal layer of cells accompanied by hyperemia and edema, and later by degeneration and desquamation of the epidermis. After larger single doses, these alterations may be marked and may extend to all the layers of the skin. The rays also act on the endothelium of the blood vessels, causing these cells and sometimes the media to swell, undergo hyperplasia, and later proliferation of connective tissue, which may lead to reduction in caliber or to actual obliteration of the vessels. This serves to explain in some measure the slow healing of radiodermatitic ulcers, an explanation further substantiated by the fact that a dose several times greater may be given to a small area of skin (1.5 to 2 cm. or less) without causing ulceration.

Besides the foregoing acute effects there exist two varieties of late effects. One variety is featured by late necrosis of the skin in a region subjected, several months or even several years before, to repeated irradiation to the point of inducing early lesions such as have been described. The necrosis commonly follows slight trauma, but may occur without any apparent, immediate cause. It begins with redness, pain, swelling and a sensation of heat, and a short time later progressive ulceration similar to that typifying early radiodermatitis of the third degree develops. Probably the chief determining cause of late ulceration is infection of the connective tissue, the natural resistance of which has been impaired by obliterative changes in the blood vessels and other chronic changes in the connective tissue itself. A second variety of late radiodermatitis is experienced by physicians or others who may have been exposed to roentgen rays at frequent intervals for a long time. Usually it affects the hands and sometimes the face. The lesions appear only after years of daily exposure and consist in thickening of the skin, with redness and sensitiveness, often also in dryness and brittleness of the nails. The skin becomes harsh and tends to crack easily, and areas of keratosis develop, which later may undergo epitheliomatous transformation. Many pioneers in roentgenology have

had the misfortune to pay for their ignorance of the danger or for their carelessness with the loss of fingers, hands or entire extremities, and a number have lost their lives.

The sensitiveness of the epithelium of mucous membranes is much the same as that of the skin. Excessive single irradiation causes first anesthesia, then dryness, redness from hyperemia, and edema. Depending on the dose, these clinical manifestations may abate and disappear or may be followed by ulceration. Repeated excessive exposures cause hyperplastic thickening of the epithelium, and this may be followed by necrosis. The radiosensitiveness of specialized mucous membranes, such as the mucosa of the stomach and intestine, varies with each structure. Irradiation of the stomach causes temporary reduction in the secretion of gastric juice, and this affects the production of hydrochloric acid and pepsin. If the stomach is exposed repeatedly at relatively short intervals, the gastric acidity and pepsin fall lower and lower, and this may continue for weeks or months. If the exposures were repeated indefinitely, the secretory activity of the gastric mucosa might be completely and permanently arrested. The susceptibility of the intestine varies in its different parts. The mucosa of the colon is relatively insensitive to the action of the rays; at least, it is much less sensitive than that of the small intestine. The most sensitive portion of the mucosa of the digestive tract is that of the duodenum and jejunum, which may be irritated by doses insufficient to disturb the overlying skin. When the upper half of the abdomen is exposed to a therapeutic dose of roentgen rays, anorexia, nausea and vomiting often follow within a few hours, and diarrhea may appear several days later. Exposure to excessive doses, such as have been employed in many experiments on animals, causes mucoid degeneration of the intestinal epithelium, hyperemia and edema of the mucosa and submucosa, and such changes may be followed by desquamation of the epithelium. According to the severity of the reaction, the epithelium may regenerate, or the breach in the mucosa may be repaired by connective tissue.

*Epithelium of the Lungs and Liver.*—The lungs are comparatively resistant to the action of roentgen rays, but if the overlying skin is exposed to a grossly excessive dose, especially if such a dose is repeated several times or if the thoracic wall is thin, reactive pneumonitis is likely to follow. This may subside spontaneously without any after effects, or may be followed by fibrous repair and by slight or marked impairment of respiratory function.

On the whole, the liver is still less radiosensitive than the lungs. Most of the pathologic changes in the liver that have been found after experimental irradiation of animals have not been a direct effect of the rays, but an indirect effect of cellular changes in other more sensitive structures. The epithelium of the biliary ducts appears to be slightly

more sensitive than the hepatic cells themselves, but it is not clear whether such alterations as have been observed resulted from a direct action of the rays, or whether they also were secondary to the circulation of toxic products of cellular degeneration in remote organs.

*Epithelium of the Kidneys.*—The kidneys can hardly be regarded as radiosensitive organs, as far as therapeutic doses of roentgen rays are concerned. Yet excessive irradiation may cause slight, moderate or severe reactive nephritis. The cells first affected are the epithelial cells of the convoluted tubules. Nephritis in radiotherapy of human beings should immediately suggest either gross overdosage or excessive elimination of toxic products of cellular degeneration in other, more sensitive structures or tissues. Certain experiments on animals have shown that, if therapeutic doses are disregarded, the organ may undergo reactive inflammation leading to chronic nephritis, with increase in blood pressure and the usual reverberations associated therewith. Such an effect merely goes to show that the kidney, like all other organs or tissues, is not wholly insensitive to irradiation but may be injured more or less severely and permanently if its tolerance is exceeded. But it must not be inferred that ordinary therapeutic irradiation of the kidneys is dangerous.

*Endothelium.*—The radiosensitiveness of the endothelium of blood vessels, pleura and peritoneum is approximately the same as that of the skin. In other words, a dose of roentgen rays insufficient to irritate the skin is not likely to have an appreciable effect on the endothelial cells. When the tolerance of the skin is exceeded, however, the endothelium is likely to suffer temporary or permanent injury. The effect of a grossly excessive dose on the blood vessels is swelling of the endothelial cells, some or all of which in the irradiated area may degenerate and desquamate into the lumen of the vessel. The media also may swell more or less. As the acute phase subsides, the destroyed cells are replaced by hyperplasia of adjacent cells that may have suffered less, and the intima or the entire wall of the vessel may thicken by hyperplasia of connective tissue. The result is a slow narrowing of the lumen, which may or may not proceed to complete obliteration. Similar changes may occur in the pleura and peritoneum. Naturally, the effect of excessive irradiation may not be confined to these structures but may extend to the underlying parenchyma of the lung or to the wall of the intestine or other tissues underlying the peritoneal endothelium. Endothelial degeneration is usually accompanied by hyperemia and serous exudation, and may subside completely or terminate by chronic adhesive pleuritis or peritonitis. If the dose of roentgen rays has been sufficiently intense, the injury to the underlying tissues may outweight the effect on the endothelium and may have

serious consequences. It is important, therefore, to keep the dose within safe therapeutic limits.

*Connective Tissue Cells.*—Young, freshly formed connective tissue cells are more sensitive, and mature connective tissue cells are less sensitive to irradiation than the epithelium of the skin. Young connective tissue, in a healing traumatic or surgical wound for example, is peculiarly sensitive to roentgen rays and, even after moderate therapeutic exposure, becomes more porous and more brittle. Moreover, moderate therapeutic irradiation of such connective tissue diminishes its formation or tends to hasten the granulation process. This effect appears to be due to the action of the rays on leukocytes infiltrating the area, and the connective tissue changes, therefore, are partly secondary or indirect; but a direct effect on the connective tissue cells also occurs. This is evidenced by the influence of roentgen rays on keloids, for which radiotherapy is the most effective treatment. Mature connective tissue cells, on the other hand, are distinctly more resistant than the epithelium of the skin, but if a dose beyond the tolerance of the skin is given, the connective tissue cells in the exposed territory may also be affected more or less. Some may be destroyed and give rise to fresh connective tissue. This probably has led to the assumption that the formation of such tissue may be stimulated by irradiation. The stimulation is never a direct result of irradiation, but is an indirect effect and always implies an antecedent destruction of cells of the same or of some other variety.

*Muscle Cells.*—The cells that typify voluntary or involuntary muscles also may be injured or destroyed by exposure to roentgen rays beyond therapeutic limits, but this involves still greater injury or destruction of the overlying tissues or implies convergence on the muscle of several beams of rays through as many separate fields. Muscle cells are comparatively resistant to the action of the rays and can readily tolerate ordinary therapeutic doses. Pathologic changes, such as the fatty degeneration sometimes observed in muscle cells after irradiation, usually result from the circulation of toxic products of cellular degeneration in other more sensitive tissues or structures.

*Bone Cells.*—Bone has long been thought impervious to the influence of roentgen rays and radium. It possesses a relatively high degree of resistance, it is true, but sufficiently intense or repeated irradiation may cause the bone cells to degenerate. The degree of such degeneration varies with the dose and with the age of the irradiated animal or person. In early life, the growth of bone can readily be retarded or permanently stopped by therapeutic irradiation, especially if the exposures are repeated. Adult bone, however, is able to tolerate rather large doses without apparent effect, but doses beyond the therapeutic

range may cause bone cells to degenerate and the bone to become devitalized. In the absence of infection, devitalized bone is slowly replaced by ingrowing new bone, especially if the affected bone is used for weight bearing. When, on the contrary, mechanical function is prevented by fracture or otherwise, the devitalized bone separates as a sequestrum, which is slowly absorbed. Secondary infection of bone devitalized by irradiation leads to the formation of a sequestrum regardless of function.

*Nerve Cells.*—As far as experimental evidence shows, the neurons of the central nervous system are the least radiosensitive of all cells. The brain and spinal cord can tolerate maximal therapeutic doses and even more with apparent impunity. But this does not mean that the specific cells of the nervous system are entirely invulnerable. Nevertheless, in many experiments on animals, in which doses several times greater than those used in the treatment of human beings were administered to the brain or spinal cord, the nerve cells did not show any perceptible evidence of a direct action of the rays. Such cellular changes as have been found after irradiation appeared to be secondary to the action of the rays on the cerebral vessels, the endothelial lining of which is more sensitive than the nerve cells themselves.

*Stimulating Effect of Irradiation.*—For years the legend that roentgen rays or radium, under certain conditions of dosage, may increase the growth and metabolism of cells has gained wide circulation. This notion has arisen from the attempt to apply to these agents the so-called Arndt-Schulz law, according to which small doses stimulate and large doses depress cellular metabolism. Based on pharmacologic grounds, this doctrine has not been generally accepted, even by pharmacologists. The attempt to apply it to the action of roentgen rays is unwarranted, because the experimental evidence on which it is based is extremely meager and apparently invalid. That a measure of acceleration in cellular metabolism may occur under certain conditions has been shown repeatedly both in animals and plants, but such unusual acceleration is a transient phase of reaction and is invariably followed by more or less pronounced cellular degeneration and inhibition of function. Another factor in the propagation of this notion of a stimulating action of the rays has been the regression of pathologic lesions after exposure to small doses of roentgen rays. Such regression is best explained by the exceptional radiosensitiveness of certain varieties of cells. As the result of primary degeneration of certain cells, a secondary or indirect stimulation may sometimes be observed. Such is the increase in connective tissue cells in certain tissues and organs after repeated irradiation; the connective tissue is laid down to replace other cells which the rays have caused to undergo degeneration. Any primary or direct

acceleration of cellular metabolism must be regarded as an effort of the cell to counteract or compensate for the noxious influence of the rays; in other words, it is purely a defense reaction. Continued acceleration of metabolism cannot be induced by roentgen rays or radium, which always cause degenerative changes or have no effect whatever. Irradiation of certain tissues, such as the skin, repeated over a long period of time may cause hyperplasia of the epithelium, and this in turn may lead to malignant transformation. This is not stimulation in the sense here employed, but alteration of a normal function to an aberrant one due to chronic irritation.

*Comparative Influence of Rays of Different Wavelength.*—Roentgen rays and radium have the same general effect on living tissue. Such variations as may be observed can be accounted for by difference in the methods of irradiation with each agent. Unfiltered radium buried in the substance of a tissue produces an intense destruction of cells immediately adjacent to the radioactive unit. The degree and extent of destruction can be modified at will by filtration. The conditions under which roentgen rays are generated precludes anything but external irradiation. If the effect of external irradiation with radium is compared with that of similar irradiation with roentgen rays, any variation attributable to difference in wavelength will be small; the greater part of the difference must be charged to variation in the total quantitative dose of each kind of energy. Quality of radiation plays a definite part in the effect, but this part is much smaller than the part played by quantity of radiation. To illustrate this further I need only draw attention to the difference of action between unfiltered roentgen rays of relatively long wavelength and rays of short wavelength generated at voltages of 80 and 200 peak kilovolts, respectively. A dose of the former beyond the tolerance of the skin to an area more than 1 inch (2.5 cm.) in diameter is likely to result in ulceration, whereas a corresponding dose of rays of short wavelength seldom causes ulceration, but usually induces a dense brawny induration of the skin and subcutaneous tissues and adhesion of the underlying muscles.

## OUTSTANDING MEDICAL IMPLICATIONS

To attempt to deal adequately with this phase of my subject would be to risk overtaxing the reader's patience. I shall confine myself, therefore, to a brief outline of the more important medical relationships.

*Radiotherapy for Inflammatory Conditions.*—Knowledge of the specific sensitiveness of different species of cells to roentgen rays or radium is of fundamental importance in the treatment of inflammatory lesions as well as in the diagnosis and treatment of certain neoplastic

processes. It has long been known that many acute or chronic, suppurative or nonsuppurative inflammations are favorably influenced by roentgen rays or radium. In some of these conditions, indeed, irradiation has been found to be the therapeutic method of choice. Among the acute inflammations amenable to such treatment may be mentioned furuncle, carbuncle, lymphadenitis, pneumonia in certain stages, parotitis and erysipelas. The more acute the process the more quickly it responds to irradiation and the smaller the dose required. Exposure of such lesions at an early stage (phase of leukocytic infiltration) usually causes them to undergo rapid resolution. Irradiation at a slightly later stage (phase of beginning suppuration) hastens the suppurative process. In both cases, but especially in the former, the course of the inflammation is shortened, and pain is quickly allayed. Usually, a single exposure to the rays is sufficient. Tuberculous lymphadenitis, tuberculosis of the cornea and iris, trachoma, actinomycosis and many diseases of the skin may be cited as examples of chronic inflammation amenable to radiotherapy. In such conditions, however, treatment must be repeated at intervals for some time. The rate and mode of reaction of inflammatory lesions indicate that the rays act chiefly by destroying the infiltrating lymphocytes, the exceptional sensitiveness of which has already been pointed out. The rate of reaction of acute inflammations corresponds so closely to the rate at which normal lymphocytes are known to be destroyed by the rays that, even in the absence of other evidence, the analogy cannot be regarded as a coincidence. Moreover, confirmatory evidence has been provided by frequent microscopic observation, in irradiated lesions of this kind, of lymphocytic destruction in every respect similar to that which was first observed and described by Heineke.

Leukocytic, and especially lymphocytic, infiltration is an early and prominent feature of most inflammatory conditions. Especially is this true in inflammations caused by bacterial infection. If it can be assumed that the leukocytes which the organism mobilizes around the site of infection represent an effort to localize the infection and get rid of the infectious material by phagocytosis or otherwise, it must be inferred that the infiltrating cells contain or elaborate within themselves the protective substances that enable them to neutralize the bacterial or other toxic products that give rise to the defensive inflammation. If these assumptions are well founded, it seems not unreasonable to deduce that irradiation, by destroying the infiltrating lymphocytes, causes the protective substances contained by such cells to be liberated and thus to be made even more readily available for defensive purposes than they were in the intact cells. All the circumstances surrounding the behavior of inflammatory lesions after irradiation are in harmony with this view. The same process also undoubtedly plays an

important part in the reaction of chronic inflammatory lesions, but in such cases the reaction is modified according to the degree of leukocytic infiltration on the one hand and to the amount of connective tissue on the other. This probably explains why the resolution and cure of chronic inflammations, such as those mentioned, require that irradiation be repeated at intervals for some time.

*Radiotherapy and the Genital Glands.*—The radiosensitiveness of the genital glands is important from more than one point of view. The relative ease with which testicular or ovarian function can be abolished by irradiation furnishes a simple method of accomplishing this result whenever such functional arrest is necessary or desirable. The method has seldom been applied to the male, but it is commonly employed in the female as an increasingly valuable method of treating hemorrhagic disturbances and fibromyoma of the uterus. Arrest of ovarian function indirectly causes atrophy of the uterus and of the fibroid tumors. In both the male and the female, roentgen rays or radium might well be utilized to castrate the feebleminded, a method that would remove the objection to surgical operation. The danger of sterilization to professional radiologists and nonprofessional technical assistants has long been realized. Fortunately, modern methods of protection, if applied, remove all danger from such employment.

*Radiotherapy for Benign and Malignant Tumors.*—The specific sensitiveness of different kinds of cells constitutes the most important single factor in the treatment of neoplasms. The value of roentgen rays or radium in the treatment of tumors of different varieties depends mainly on this feature. The susceptibility of tumors to irradiation agrees closely with the radiosensitiveness of normal cells of the same kind as those from which the tumors are derived and of which they are largely composed. Thus, the inordinate hyperplasia of lymphoid structures that characterizes Hodgkin's disease, lymphosarcoma and lymphatic leukemia retrogresses under irradiation at the same rate as normal lymphocytes are known to be destroyed by similar exposure. In fact, so striking is the parallel that irradiation is now being used daily as a means of distinguishing such conditions when their clinical features do not permit absolute identification. In some cases, indeed, the radiotherapeutic method of diagnosis is more accurate and dependable than microscopic examination.

The only tumor that approaches lymphogranuloma or lymphoblastoma in susceptibility to irradiation is the embryonal carcinoma, or seminoma, of the testis, the radiosensitiveness of which corresponds to that of normal spermatogonial cells. This is the most common neoplasm affecting the organ. Heretofore it has often been mistakenly regarded as a variety of sarcoma. Primary and secondary growths of

this kind retrogress rapidly and some disappear completely, though seldom permanently, after irradiation. The rate of regression is not quite so rapid as that of lymphoid tumors, but next to that is more rapid than the rate of any other variety of tumor. The reaction of mixed, or teratoid, tumors of the testis is less rapid and seems to vary with the proportion of spermatogonial epithelium entering into their structure. The clinical features of testicular tumors and the path and elective sites of metastasis are usually so characteristic as to make confusion with lymphoid tumors all but impossible.

Knowledge of the relative radiosensitiveness of different cells has enabled Ewing and others to distinguish a group of bone tumors from other neoplasms that affect the skeleton. Ewing has designated this tumor as diffuse endothelioma of bone because endothelial cells are a prominent feature, but it is more widely known under the term endothelial myeloma applied to it by Kolodny and others. Unlike all other tumors of bone, the diffuse endothelioma of Ewing is exceptionally sensitive to radium and roentgen rays. Indeed, the exceptional susceptibility of this tumor to irradiation was one of the peculiarities that convinced Ewing that this variety of neoplastic disease is entirely different from osteogenic sarcoma. The rate at which such neoplasms retrogress after exposure to the rays suggests a more than coincidental relation to lymphogenous disorders, such as those observed in lymphoblastoma. The rate of regression of endothelioma so closely approximates that of lymphosarcoma or Hodgkin's disease that one is led to infer a definite relationship. At any rate, among tumors of bone the susceptibility is quite exceptional. The only other tumor of bone that can be said to be radiosensitive is chondrosarcoma, but the susceptibility of the latter variety is much less than that of the former. The difference is so great that confusion is practically impossible. Osteogenic sarcoma, on the contrary, can hardly be said to be radiosensitive. Rather, it is characterized by its resistance to irradiation. Few such tumors can be made to retrogress to an appreciable degree, even by the most intense irradiation. In fact, increasing experience with radiotherapy for tumors of bone makes it seem more and more likely that, whenever such a tumor proves unusually sensitive and diminishes rapidly in size or disappears temporarily or permanently after irradiation, it is an endothelioma, regardless of any classification based on microscopic appearance.

Another tumor of bone the radiosensitiveness of which is usually so characteristic as to constitute a valuable diagnostic sign is the so-called benign giant cell tumor. Two or three weeks after irradiation, the growth, instead of undergoing gradual retrogression for a time, or remaining unaffected, as do all malignant neoplasms of bone or soft tissues, begins to swell, and the swelling is accompanied by redness and

pain. This may continue for a number of weeks. If the patient or the attending physician has not been forewarned, he may quite naturally conclude that the rays have actually stimulated the tumor to increased growth, and this assumption may result in unnecessary sacrifice of the affected limb. After from three to six weeks, this acute reaction subsides spontaneously, and after the lapse of several months roentgenograms of the bone generally show deposition of fresh bone. In time, the entire tumor is replaced by solid bone. This kind of reaction differs entirely from the behavior of malignant tumors and supports the view that giant cell growths are chronic inflammatory lesions, at least at the outset. The fact that some of these tumors ultimately acquire malignant features does not affect the apparent validity of this deduction. All true tumors, benign as well as malignant, retrogress rapidly or slowly, remain stationary, or continue to grow at the same rate as before irradiation.

Many other examples might be mentioned, but these are sufficient to illustrate the important bearing on medical diagnosis and treatment of the radiosensitiveness of cells and tissues. Heretofore, for some reason, biologists have seldom made use of radiation for experimental purposes. As soon as they begin to realize its possibilities they will find in the method a means of acquiring much valuable information, and such increase in knowledge will help to extend the diagnostic and therapeutic applications.

# ENTEROSTOMY

## A CONSIDERATION OF THE LITERATURE

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### THE EARLIER LITERATURE

Enterostomy was recommended by Fuhr and Wesener in 1886 as a useful measure in the treatment for intestinal obstruction. For cases in which the obstruction was not readily relieved or the patient's condition did not permit an extensive operative procedure, its use was advised for temporary relief. A distended loop of intestine was brought up into the incision and sutured to the peritoneum.

The use of this measure was quite widespread from 1880 to 1900. The technic was that described or it varied in that the loop was brought out to the skin, or it consisted of either of these methods with the addition that a glass tube was fastened into the intestine.

The apparent success of this form of treatment in cases of mechanical ileus suggested its possible value in certain cases of appendicitis. It was noted that in some cases of appendicitis there was marked distention, and that in others following the operation for appendicitis great distention occurred. The mortality was very high in these two groups of cases.

Porter, in 1897, reported a case in which he performed enterostomy for the distention associated with appendicitis, with recovery of the patient. (For additional early references to enterostomy in the United States see references to Hadra and Henrotin.) Heidenhain's papers, published in 1902, in which he reported five cases in which enterostomy was done for ileus following operation for appendicitis, with four recoveries, are quoted in the German literature as the inception of this measure as a generally accepted procedure. Lund, in 1903, reported five cases with four recoveries. Tinker, Bullitt, Dunsmore and Porter, in their discussions on Lund's paper, stated that they considered this procedure a life-saving measure which they had used to a limited extent.

Thomas is the only person whose objections to this measure were found in the literature of this period. He stated that he considered

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This is a preliminary paper which is to be followed by a statistical consideration of the subject.

that those patients who recovered after an enterostomy would have done so without the operation. He quoted Nicholas Senn as teaching the same belief.

Broca appears to be the first in the French literature to have recommended the use of enterostomy for intestinal obstruction following appendicitis. His paper was published in 1901, and a case with recovery was reported.

Following Heidenhain's papers, the use of enterostomy became quite widespread in Germany. Gebhardt, in 1904, recommended its use not only in the treatment of postappendical obstruction but as a prophylactic measure in certain cases of appendicitis. In the discussion of appendicitis and peritonitis at the German Surgical Congress in 1909, enterostomy was recommended by Barth, Alapý and Hoffmeister. Krogius, in 1911, reported seventy cases in which he had performed the operation between 1900 and 1911 with twenty-three recoveries.

In 1921, Brunner reported thirty-four cases with ten recoveries; Wortmann, twenty-seven cases with twenty-two recoveries; Dubs, twenty-four cases with six recoveries. Eliot and Pickhardt, in 1921, reported four cases in which ileostomy had been done for obstruction following appendicitis in 1907, with three recoveries.

Sick, in 1908, and again in 1909, published articles in which he questioned whether or not the efficacy of this measure had been proved.

From 1921 on, particularly from 1925 to 1928, papers on enterostomy occur very frequently in the literature of Germany, Italy, France, Great Britain and the United States. A representative list of these will be found at the end of the paper.

With almost no exception the procedure is recommended. In a great many of the papers no cases or statistics are cited to back up the recommendation, the reason usually cited being that some other surgeons thought it a successful form of treatment. Many others cite from one to ten cases in which all or part of the patients recovered. None of them give any suggestion of a method for determining which of the patients who recovered might have been expected to survive without enterostomy.

The few criticisms found in the literature other than those already mentioned will be taken up later.

## EXPERIMENTAL RESULTS

Before entering into a further consideration of the literature on enterostomy, it might be well to review briefly the results of some of the experimental work on intestinal obstruction and peritonitis.

McClure, in 1907, showed that the stagnant contents of obstructed loops form an excellent culture medium which soon becomes loaded with bacteria. The bacterial content could be slight at the time of

closure, but multiplication was extremely rapid. This rich bacterial growth not only provided the gas which damaged the bowel by overdistention but also invaded the strangulated tissues causing septic gangrene. McClure thought that there was no absorption until the intestinal wall was damaged.

Albeck, in 1901, Murphy and Brooks, in 1915, and many other observers since, recognized the occurrence of a toxic substance within the bowel but emphasized the fact that absorption of the toxin did not occur through the normal intestinal epithelium. Davis, in 1914, and Schonbauer, Stone, Whipple and Wilkie later demonstrated that large amounts of this toxin may be introduced into the lumen of the normal small intestine with no untoward results.

L. R. Dragstedt, Moorehead and Burcky, in 1917, found that closed loops of the jejunum were fatal within from three to four days. If the isolated loop, instead of being closed, was washed and left open into the peritoneal cavity, those dogs that survived the peritonitis remained well. In a few weeks the loop was found to be sterile and was then closed without causing toxic symptoms, although the loop became distended and in some cases even ruptured. In these sterile loops, when the blood supply was entirely occluded, anemic necrosis developed. In the absence of bacteria this process caused no toxemia.

L. R. Dragstedt, C. A. Dragstedt, McClintock and Chase, in 1919, found that washing the closed loop with ether, alum or tannic acid so affected the loop that it would not absorb the toxic products, but that bacterial action went on unchanged.

Gerard, in 1922, stated that the contents of an obstructed bowel become poisonous as a result of the formation of histamine and allied proteolytic products by the action of putrefactive bacteria.

Haden and Orr, in 1923, reported that they were able to keep dogs with pyloric or intestinal obstruction alive for from twenty to thirty days by the hypodermic administration of sodium chloride solution.

Gamble and Ross, in 1925, found the cause of death in pyloric obstruction to be the loss of sodium and chloride ions by vomiting. This loss resulted in the inability of the body tissues to retain water. The resulting dehydration combined with starvation caused the death of the dogs. The authors found that the treatment with saline by hypodermoclysis, intravenously or through an enterostomy opening, kept the dogs alive.

Orr and Haden in 1926, reported that in the dog they found that the chemical changes in the blood characteristic of acute obstruction of the jejunum are not prevented by jejunostomy. They found no beneficial effect on the duration of life. Sodium chloride solution tended to prolong life in acute obstruction of the jejunum with or without jejunostomy. Simple jejunostomy killed the animals quicker than the obstruction.

The same authors, in 1929, reported the same chemical changes in the blood in peritonitis as those found in intestinal obstruction, i. e., an increase in nonprotein and urea nitrogen, a decrease in chlorides and no constant change in the carbon dioxide-combining powers.

Experimental peritonitis without treatment was fatal in their first series in three and one-eighth days; in their second series, in four and one-eighth days. When treated with ileostomy plus 40 cc. of a 1 per cent solution of sodium chloride per kilogram of body weight, the average life was extended to ten and one-third days. With ileostomy alone, they reported no lengthening of life.

In 1926, they reported that drainage of the jejunum in dogs caused death in from two to five days, even though the fluids and chlorides lost were replaced in some manner. Drainage of the ileum 6 inches (15.2 cm.) above the cecum was found compatible with life in dogs for several weeks. They concluded from these experiments that enterostomy (in the ileum) should be done when the symptoms of obstruction appear with peritonitis in the lower part of the abdomen, provided the intestine above shows signs of peristaltic action. In case of doubt they recommended enterostomy as it does no harm and may do good. They stated that in addition large quantities of saline should be used.

Hausler and Foster, in 1924, came to the following conclusions in experimental intestinal obstruction:

"Experimental intestinal obstruction may be classified as acute simple obstruction and acute strangulation obstruction. The pathology and lethal factors are definitely different in the two classes." In the first class they found only slight changes in the pulse, temperature, respiration and blood pressure. In the second class they found profound changes in all of these factors. They stated that from 30 to 40 per cent of cases of acute ileus belong to the first class, but that if they are neglected they go to the second class.

Hartwell and Cooper, in summing up the experimental work on the toxemia of intestinal obstruction, stated:

(1) In high obstruction there are two different processes involved. First, there is a profound disturbance in the acid-base mechanism resulting in alkalosis and dehydration. Secondly, there is a definite toxemia. In simple obstruction this first process is the more prominent and often fills the whole picture. However, toxemia may enter also to a varying extent. On the other hand, in closed loops and strangulation the toxemia is on the ascendancy and often crowds everything else out.

(2) There is a toxin in the lumen of the obstructed gut and it looks very much as though it reached the blood stream and was responsible for the toxemia. The origin of this toxin is not entirely clear. Those who say that it is formed by bacteria must show:

(*a*) Why high obstruction is more fatal than low.

(*b*) Why the toxin appears so rapidly after obstruction.

(*c*) Why the toxin appears in the gut immediately after toxic injection.

(*d*) Why the toxin appears in such conditions as clotting of the portal vein, acute pancreatitis and bilateral adrenalectomy, where there is no obstruction.

Those who claim that it is not formed by bacteria have to prove its formation in their absence.

(3) There seems to be some mysterious connection between the toxemia of high obstruction, acute pancreatitis, bilateral adrenalectomy and anaphylaxis.

. . . We should like to emphasize the fact that more work should be done on strangulation. Here we have the toxemia developed to the highest degree. We are able to control the alkalosis and dehydration. However, it is very rare to see simple obstruction in the clinics without the complication of toxemia. Therefore, it remains to find a means of combatting this dread condition.

They have appended to their discussion a very comprehensive list of references on the experimental work done with intestinal obstruction.

## EMPTYING THE BOWEL AT OPERATION

From a consideration of part of these experimental results it is easy to arrive at the conclusion that the obstructed loop or loops should be emptied as promptly as possible. Some men go even a step farther and conclude that the contents should be removed from the patient at the time of the operation. These men do not take into account the experimental finding that the toxins apparently are not absorbed through normal intestinal mucosa.

Stone recommended that the contents of the bowel be removed at the time of operation and that the intestine be freely irrigated with large quantities of distilled water. He cited no clinical material or statistics to back up his recommendation.

Holden advised emptying the bowel at the time of operation, and then closing the opening through which it was emptied. He used a flanged glass tube for emptying the intestine. He stated that his mortality figures in intestinal obstruction had been lowered 10 per cent by this practice.

Cornils, in 1926, described a very complicated apparatus for emptying the intestine at operation. Cambresier advised the puncture and drainage of the intestine or enterostomy as the treatment for postoperative paralytic ileus. Willis advised in some cases of obstruction that the bowel be punctured, drained and the opening then closed.

Flörcken gave comparative figures which are most interesting in a consideration of this emptying operation (table 1).

He concluded that emptying at the time of operation should not be done, but that enterostomy was of value when the intestine showed contractility. He did not state whether or not the emptying was done on the worst cases, which of course is a possibility and would remove some of the teeth from his argument.

### ILEOCOLOSTOMY, JEJUNOCOLOSTOMY AND CECOSTOMY IN PERITONITIS

While ileostomy and jejunostomy were being tried out as forms of treatment for ileus following operations for peritonitis, another mechanical treatment was suggested by Sampson-Handley in 1915 and again in 1916. He advised jejunocolostomy to short-circuit the involved area and with this a cecostomy to drain the obstructed cecum and terminal ileum. He thought jejunostomy was inadvisable.

Nyulasy, in 1917, recommended cecostomy alone as the treatment for intestinal paralysis subsequent to operations for peritonitis. He felt that the stasis was not complete. Roeder believed that in operations for appendicitis with peritonitis, when the cecal region is thickened and indurated, that region should be side-traced by doing an ileosigmoidostomy. He reported twenty-one such operations with twenty recoveries. Deaver likewise recommended that, when the terminal ileum and cecum

TABLE 1.—*Data of Flörcken*

| | Cases | Died | Mortality, per Cent |
|---|---|---|---|
| Strangulation ileus | 41 | 7 | 17 |
| Emptied at operation | 7 | 4 | 57 |
| Not emptied | 34 | 3 | 9 |
| Volvulus, invagination, gallstone ileus, etc. | 17 | 8 | 47 |
| Emptied at operation | 4 | 4 | 100 |
| Not emptied | 13 | 4 | 30 |

are found indurated when operating for an appendical abscess, either an ileocolostomy or ileocecostomy be done.

Voncken advised that in obstructions following operations for acute appendicitis a cecostomy be done if the cecum is found distended. However, in three of his cases cecostomy gave no relief, and ileostomy was performed the following day. Two of these patients recovered.

Duncombe advised ileocolostomy combined with the use of hypertonic salt solution intravenously. He reported recovery in one case after this treatment.

### ENTEROSTOMY IN MECHANICAL ILEUS

The use of enterostomy as a useful adjunct in the treatment for mechanical ileus has been more or less accepted in the literature since 1880. From 1910 on, this became somewhat limited to jejunostomy although ileostomy was also recommended frequently.

Between 1920 and 1925, jejunostomy was advised in the treatment for mechanical ileus by C. H. Mayo, Wilkie, Taylor, Walker, Summers, Lee and Downs, and Delore, Mallet-Guy and Creyssel. This list is given only as representative of the large literature on the subject.

### JEJUNOSTOMY IN PERITONITIS

While the teaching of enterostomy, but more particularly of ileostomy as treatment for ileus and peritonitis was spreading gradually from the original recommendation of Heidenhain, Victor Bonney came out in 1910 with a very definite recommendation that jejunostomy be used instead. In 1916, he wrote: "I hold strongly that all cases of paralytic obstruction whether primary or secondary to an organic obstruction or to peritonitis, when advanced to the stage of fecal vomiting, should be treated by jejunostomy. The effect in many cases has been remarkable."

Papers in addition to those specifically mentioned in which jejunostomy and ileostomy are discussed and recommended are listed at the end of this article.

Its success in the treatment for mechanical obstruction developing from two to twenty days after operation for the peritonitis of appendicitis or other causes appears quite general in these reports. Ordinarily the obstruction disappears as the inflammatory processes subside, and in those cases in which the obstruction is due to a band or other cause not spontaneously relieved the patient is carried through the critical time, and the obstruction can then be relieved with the patient in condition to withstand the operation.

### PARALYTIC ILEUS

In the paralytic type of ileus various authors report good results with jejunostomy, although the majority qualify this with the limitation that the jejunum must show active peristalsis. Here, of course, the reported cases are subject to question, not as to cure but as to the classification of the type of ileus. Wilkie, in 1928, stated that a postmortem study of a series of patients dying from so-called peritonitis or paralytic ileus from five to ten days after operations for acute appendicitis showed the cause of death to be mechanical intestinal obstruction in 75 per cent. This suggests that those cases of paralytic ileus in which jejunostomy was successful were in reality cases of mechanical ileus. But, possibly, this further suggests that one cannot clinically separate mechanical and paralytic ileus after operations for peritonitis and that one should give the patient the benefit of the doubt and a jejunostomy.

### MEDICAL TREATMENT FOR POSTOPERATIVE ILEUS

The close observation and study of the patients making up any large series of cases of peritonitis will reveal a considerable number of patients who have a partial paralytic ileus or a temporarily complete one, who recover without additional surgical procedures. The question may be brought up as to whether or not those patients successfully treated by enterostomy do not belong to this class now under discussion.

Of course, the remarkably rapid and complete recovery of these patients, who before operation appeared in extremis, is given as the answer to this question, but this is not as conclusive as statistics would be.

This brings one to the medical treatment for postoperative ileus. This has not been given the consideration due such an important subject, although a great deal of medical treatment for postoperative ileus is done without the physician stopping to realize that that is what he is treating.

It is very difficult to draw the line between the nausea and distention due to ether, to handling of the intestine, to the irritation of peritonitis or other similar temporary cause and that of beginning ileus. In fact, they are probably one and the same thing.

The medical treatment includes stomach lavage, spinal anesthesia in the spastic paralysis, anal dilatation, pituitary extract, atropine, morphine, sodium chloride, dextrose, water and the use of the rectal tube and flaxseed poultices. As the patient becomes more ill, one must add the use of camphor, caffeine and other stimulants.

The Einhorn tube and the duodenal bucket have been used with success. The more recent addition of the Levine tube has made the treatment much simpler and surer. It may be put down, left in place, and then irrigated every hour or half hour with physiologic solution of sodium chloride. Gastric dilatation is prevented, the upper part of the intestine is emptied by reverse peristalsis and undoubtedly some water and salt are supplied to the patient. Additional operation is often averted in this manner. This is recommended by Jancke and others.

J. H. Woolsey stated that the duodenal tube will accomplish all that jejunostomy does. Likewise, Romano and Rey reported the successful use of the duodenal tube instead of ileostomy or jejunostomy in treatment for the uncontrollable vomiting of bacterial peritonitis.

Sick, in 1908, doubted whether primary enterostomy was of value in intestinal obstruction and volvulus. In 1909, he added to this that he felt the treatment for peritonitis by primary enterostomy was of very questionable value. He considered early diagnosis and operation followed by the various medical treatments of much greater value in reducing the mortality figures. He felt that the inanition, additional shock, possibility of infection and necessity of closing the fistula contraindicated enterostomy in purely mechanical obstruction.

Eisberg considered jejunostomy as contraindicated in mechanical ileus, stating that it causes death, and if the patient recovers a secondary operation is necessary.

### SURGICAL TREATMENT FOR POSTOPERATIVE ILEUS

However, cases will be found in which medical treatment, even including the thorough and proper use of the Levine tube, will give no

relief. A considerable percentage of these cases will be due to mechanical obstruction. Operative intervention as soon as diagnosis is made and other treatments fail will give a high percentage of recoveries. If the patient's condition and the nature of the obstruction permit, removal of the cause is indicated. Otherwise a jejunostomy should be done. A later relief of the mechanical obstruction may be necessary in a few of these cases.

The generally accepted manner of doing the jejunostomy at the present time appears to be as follows:

Under local anesthesia, a short incision is made in the left upper quadrant lateral to the rectus muscle. The loop of small intestine immediately beneath the incision is brought up into the incision. The time and trauma involved in locating definitely a loop of jejunum are rarely justified.

The end of a large-sized soft rubber catheter is fixed in the lumen of the intestine either by two purse-string sutures or by the Witzel method. The catheter is then drawn through a small hole in the omentum and the omentum drawn up against the parietal peritoneum. The wound is closed about the catheter in layers, or if the patient's condition is precarious, may be closed with through-and-through sutures.

If the jejunostomy or ileostomy is done at the same time as another operation, the same procedure is used in inserting the catheter and bringing it through the omentum. A small stab wound is then made to the left of and above the umbilicus, and the catheter is then drawn out through this wound.

When the jejunostomy is done, it must not be left to cure the patient unaided. Irrigation should be done every hour or half hour with physiologic solution of sodium chloride. Salt and dextrose solutions should be given in large quantities by infusion or hypodermoclysis. Other treatments should be used as the indications arise.

As soon as clear contents without odor replace the turbid foul return which is obtained at first, and the distention is relieved, the tube is clamped and used for the introduction of salt solution and if necessary for nutrition. From the fourth to seventh day the tube will come away, and by the tenth to fifteenth day the sinus tract will close.

The remainder of the patients under consideration compose the group with paralytic ileus. If the condition is advanced and complete, even with jejunostomy the mortality is high. Whether or not jejunostomy lowers the death rate is a question and many authors feel that it is of no benefit. Most of those who do recommend it qualify this with the reservation that the jejunum must show contractility.

The evaluation of the results of jejunostomy in this class of cases is extremely difficult. First, there is the doubt as to the correct diagnosis; and, second, how can one be sure that those patients who recover would not have done so without enterostomy; and, furthermore, that some of those not surviving might have done so without the enterostomy.

I feel that at present no figures or statistics are available to argue for or against this form of treatment of ileus, but that the indications are, that if one can be certain he is not dealing with a mechanical ileus, enterostomy is probably of little use.

### PRIMARY OR COMPLEMENTAL ENTEROSTOMY

Opinions as to the value of complemental enterostomy can be cited, but facts and figures are a different thing. The following is typical of the unlimited recommendation of enterostomy not backed by any statistics. Holman stated:

> Ileostomy or enterostomy is indicated in severe cases of ruptured appendix with spreading peritonitis, in intestinal obstruction, peritonitis due to ruptured viscus or perforated bowel, postoperative ileus, traumatic peritonitis, pneumococcic or streptococcic peritonitis and in certain cases of intestinal anastomosis or resection of the bowel.

McKinnon, in 1928, stated that he not only treats patients with postoperative ileus by jejunostomy but does it at the time of operation in those cases in which ileus is expected to develop. He gives no statistics as to the decreased occurrence of postoperative ileus since starting this usage.

Clute stated:

> Peritonitis gives paralysis of the involved gut and the result simulates obstruction because the loops above cannot empty.

He concluded from his own cases that:

> Enterostomy in acute intestinal obstruction is of great value when it removes the toxic products collected above the point of obstruction. Drainage of the large intestine in low obstruction gave excellent results. Drainage of the jejunum in acute obstruction gave good results. Septic peritonitis produces death largely from toxemia arising from the infection plus the products of the intestinal obstruction caused by the paralysis of the gut. Caecostomy in peritonitis gave very poor results; jejunostomy quite satisfactory results. Jejunostomy should be added to our present methods for the treatment of diffuse septic peritonitis.

Whipple stated in 1927 that:

> In dynamic ileus and paralytic ileus with peritonitis—where much distention of the small intestine and fecal vomiting are present—high ileostomy or jejunostomy is a life-saving measure. . . . An increase in enterostomies of 63 per cent gave a 13.2 per cent reduction in mortality.

He referred to a paper to be published later by Van Beuren and Smith (August, 1927). Comparative statistics on operation for ileus before and after 1900, as quoted by these authors, are shown in table 2.

The reductions in mortality would be readily accounted for by improvement in surgical technic and hospital regimen. The great increase in enterostomies performed, nearly double, should have resulted in a great decrease in the total mortality if it is the life-saving measure that it has been reported to be.

Comparison of mortality figures in peritonitis and obstruction operations in groups with enterostomies and those without always gives lower mortality in the groups not including enterostomies. The argument raised against this is that enterostomy is always saved as a procedure of last resort.

The only method of final evaluation for enterostomy would be to compare the mortality statistics in peritonitis and ileus obtained from

TABLE 2.—*Data of Van Beuren and Smith* *

| | Number of Cases | | Mortality Percentage | |
|---|---|---|---|---|
| | Series 1900 | Series 1925 | Series 1900 | Series 1925 |
| Entire series | 1,000 | 1,089 | 43.2 | 41.8 |
| Nonenterostomy group | 810 | 740 | 32.2 | 33.0 |
| Enterostomy group | 190 | 349 | 64.2 | 60.7 |

* One thousand cases compiled by C. D. Gibson, 1900; 1,089 cases compiled by Van Beuren and Smith, 1925.

various hospitals, comparing the figures from hospitals in which the staff does few or no enterostomies with the figures from those hospitals in which it is used as a routine measure.

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# ACUTE PANCREATITIS

## REPORT OF SIXTY-FOUR CASES

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This study is based on all the available records of patients with acute pancreatitis who were treated by members of the Chicago Surgical Society.[1]

The following classification has been found satisfactory:

*A.* Acute idiopathic pancreatitis
1. Simple edematous or nonhemorrhagic pancreatitis
2. Hemorrhagic pancreatitis
3. Necrotic or gangrenous pancreatitis
4. Suppurative pancreatitis

*B.* Acute pancreatitis associated with malignancy

*C.* Acute pancreatitis following trauma

Fitz [2] classified acute pancreatitis into hemorrhagic, suppurative and gangrenous. Brocq [3] classified it as aseptic and infected. He included four degrees of aseptic pancreatitis: acute hemorrhagic, edematous, subacute encysted and attenuated. Brocq considered gangrenous pancreatitis as infected with anaerobic, and the suppurative type as infected with pyogenic, bacteria.

In 1856, Bernard [4] reported the production of an acute hemorrhagic pancreatitis following the experimental injection of bile and sweet oil

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1. Case reports from members of the Chicago Surgical Society. No cases are included after May, 1924. The cases were reported by: Edmund Andrews, Arthur D. Bevan, Carl Beck, E. J. Brougham, Gatewood, John A. Graham, W. T. Harsha, Harry Jackson, Charles E. Kahlke, Allen B. Kanavel, Dean D. Lewis, R. W. McNealy, G. L. McWhorter, Carl Meyer, Edwin M. Miller, Paul Morf, O. E. Nadeau, John Nuzum, A. J. Ochsner, Nelson M. Percy, D. B. Phemister, H. M. Richter, H. M. Riebel, C. C. Rogers, Charles F. Sawyer, William Schroeder, V. C. Schrager, Joseph Smith, D. C. Straus, George de Tarnowsky, Roger T. Vaughan and John A. Wolfer.

2. Fitz, R.: Acute Pancreatitis, M. Rec. **35**:197, 1889.

3. Brocq, P.: Les pancréatites aiguës chirurgicales, Paris, Masson et Cie, 1926.

4. Bernard, Claude: Mémoire sur le pancréas, Compt. rend. Acad. d. sc., 1856, supp. 379.

into the pancreatic duct, with death after eighteen hours. Many other substances produced similar results.

Considerable progress has been made through experimental study and by more general clinical recognition of acute pancreatitis, but owing to its infrequent occurrence and to the relatively difficult diagnosis, little progress has been made in reducing the incidence or in lowering the mortality due to this highly fatal condition.

The following classification of the etiology of acute pancreatitis may be advocated.

*A.* Infectious origin
1. By extension along the lymphatics
2. By extension from the blood stream
3. By extension along the pancreatic ducts from the duodenum or from the bile tracts
4. By direct extension from infected foci
5. Following activation of bacteria in the normal gland
6. By bacterial permeability from adjacent altered viscera

*B.* Noninfectious origin
1. Mechanical, including stasis in the ducts
2. Chemical and originating in activated ferments, resulting from
   (*a*) Bile
   (*b*) Duodenal contents
   (*c*) Degenerated duct contents
   (*d*) Autolysis
3. Degenerative changes in the pancreas
   (*a*) Secondary to benign or malignant tumors
   (*b*) Resulting from vascular degeneration or hemorrhage
   (*c*) Toxic changes following systemic disease
4. Trauma

*C.* A combination of two or more of the factors

Infection, either directly or indirectly, may be a factor in acute pancreatitis (Barling [5] and Wolfer [6]). The bacteria found most frequently include the colon bacillus, the pneumococcus and the staphylococcus. While Brocq found anaerobic bacteria in the gangrenous type of acute pancreatitis, he found that the necrotic and subacute types were sterile.

Truhart [7] collected eighty records of careful bacteriologic examinations in cases of acute pancreatitis. No bacteria were found in forty-three instances, while in thirty-seven cases bacteria were obtained from

5. Barling, G.: An Address on Pancreatitis and Its Association with Cholecystitis and Gallstones, Brit. M. J. **1**:705, 1923.

6. Wolfer, J. A.: Practical Points in Diagnosis and Treatment of Acute Pancreatitis, Illinois M. J. **41**:14 (Jan.) 1926; recent unpublished paper.

7. Truhart, H.: Pankreas-Pathologie: Multiple abdominale Fettgewebsnekrose, Weisbaden, J. F. Bergmann, 1902; quoted by Opie, E. L.: Diseases of the Pancreas, Philadelphia, J. B. Lippincott, 1910.

the pancreas, the peritoneal fluid or from foci of necrosis. Numerous micrococci were found ten times, bacilli, mostly colon bacilli, twenty-two times, and unidentified organisms in the other cases. In acute necrosis of the pancreas, Jones [8] was unable to find bacteria in smears or cultures.

Experimentally, Carnot,[9] Hlava,[10] Körte [11] and others have been able to produce hemorrhagic, suppurative and sclerosing types of pancreatitis by injecting into the duct colon, pyocyaneous and other bacteria. Archibald and Brow [12] after injecting the colon bacillus, observed a very fatal type of acute pancreatitis. Kemp [13] stated that certain bacteria, especially of the typhoid and colon group, are capable of activating the proteolytic pancreatic enzymes.

The lymphatic route of infection from the gallbladder, liver and the appendix has been emphasized in both acute and chronic pancreatitis (Graham and Peterman [14] and Barber [15]), but the acute type has not been produced experimentally by this route (Jones). The lymphatics of the pancreas have been shown by numerous writers to anastomose freely with those of the surrounding viscera, especially with those of the duodenum and gallbladder. Franke [16] has injected the lymphatics about the head of the pancreas from those of the gallbladder, which has been considered the chief source of infection by Maugeret,[17] Arnsperger,[18] Deaver,[19] Graham, Judd [20] and Griffiths.[21]

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8. Jones, F.: S. Clin. North America **2**:1125 (Aug.) 1922; Acute Pancreatitis, Boston M. & S. J. **186**:337, 1922.

9. Carnot, P.: Maladies des glandes salivaires et du pancréas, Paris, J. B. Baillière et fils, 1908, p. 109.

10. Hlava, quoted by Opie (footnote 7).

11. Körte, W.: Cong. de la Soc. internat. de chir., Bruxelles, Sept. 1911; quoted by Brocq (footnote 3).

12. Archibald, E., and Brow: The Experimental Production of Pancreatitis in Animals as the Result of the Resistance of the Common Duct Sphincter, Surg., Gynec. & Obst. **28**:529 (June) 1919.

13. Kemp, R. C.: Diseases of the Stomach and Intestines, ed. 3, Philadelphia, W. B. Saunders Company, 1917.

14. Graham, E. A., and Peterman, M. G.: Further Observations on the Lymphatic Origin of Cholecystitis, Choledochitis and Associated Pancreatitis, Arch. Surg. **4**:23 (Jan.) 1922.

15. Barber, H.: New York State J. Med. **22**:543, 1922.

16. Franke: Deutsche Ztschr. f. Chir. **111**:539 (Sept.) 1911; **54**:399, 1900.

17. Maugeret: Thèse de Docteur, Paris, 1898, quoted by Archibald, E.: Internat. Clin. **2**:1, 1918.

18. Arnsperger: München. med. Wchnschr. **68**:729, 1911.

19. Deaver, J.: Pancreatic Lymphangitis, Surg., Gynec. & Obst. **28**:433 (May) 1919; Pancreatitis, S. Clin. North America **1**:1, 1921; Ann. Surg. **68**:281, 1918.

20. Judd, E. S.: The Relation of the Liver and the Pancreas to Infection of the Gallbladder, J. A. M. A. **77**:197 (July 16) 1921.

21. Griffiths, H. E.: Lancet **2**:203, 1904.

In 1,290 cases of gallbladder disease, Judd found an associated chronic pancreatitis in 26.8 per cent. Mayo-Robson [22] found changes in the pancreas in 60 per cent of cases with gallstones, and Quenu and Duval [23] found changes in 50 per cent. Jones believed that chronic pancreatitis was an inflammation of the interstitial tissue frequently occurring by way of the lymphatics, while acute pancreatitis was an involvement of the parenchymal cells occurring by way of the ducts.

Infection may be carried to the liver from the gastro-intestinal tract by the portal system and produce pancreatitis by a descending infection as believed by Stockton.[24] The hematogenous route of infection may produce acute pancreatitis either by bacterial metastases or by extension along the blood vessels, as thrombophlebitis, from the foci of infection.

As a sequel to epidemic parotitis, the occurrence of acute pancreatitis has been recognized for a long time (Oser [25]). Farnham [26] and Edgecombe [27] have reported cases complicating mumps. Farnham collected 119 cases. The disease occurred more often in boys and young men, and occasionally preceded the parotitis.

Experimentally, Rosenow [28] injected intravenously a streptococcus obtained from the tonsils of a patient having symptoms of inflammation of the gallbladder and pancreas, and obtained lesions in those organs, although with other strains of streptococci lesions of the pancreas were rare.

Extension of infection may occur along the chief pancreatic duct from the bile tracts or from the duodenum directly up either pancreatic duct. Downward infection from the bile by direct reflux into the pancreas may occur. Infection may also occur from a focus in the duodenum, and extend up either pancreatic duct or, possibly, by a reflux of duodenal contents.

It is probable that stasis in the pancreatic duct, either alone or together with a reflux of bile into the duct is a contributing factor to the development or extension of infection in the pancreas. Direct extension of infection from adjacent foci may result from various types of acute inflammation.

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22. Mayo-Robson: Lancet **1**:773, 1904.
23. Quenu and Duval: Rev. de chir., Paris **32**:401, 1905.
24. Stockton: Gastrointestinal Infection in Relation to Infection of the Liver and Bile Passages, Am. J. M. Sc. **163**:485 (April) 1922.
25. Oser, L., in Nothnagel: Encyclopedia of Practical Medicine, Philadelphia, W. B. Saunders & Company, 1905.
26. Farnham, L. W.: Pancreatitis Following Mumps, Am. J. M. Sc. **163**:859 (Oct.) 1922.
27. Edgecombe: Practitioner **80**:194 (Feb.) 1908.
28. Rosenow, E. C.: Focal Infection and Elective Localization of Bacteria in Appendicitis, Ulcer of the Stomach, Cholecystitis and Pancreatitis, Surg., Gynec. & Obst. **33**:19 (July) 1921.

Bile (Tatum [29]) or intestinal contents, such as from a perforated duodenal ulcer (Richter [30]), may produce an acute pancreatitis. Bacteria may be present in the normal liver and pancreas, as was shown in animals by Tower [31] and Dragstedt.[32] Tower was unable to produce a sterile pancreatitis. Patrie, Pyle and Vale,[33] after a direct anastomosis of the pancreatic duct, experimentally, with both the small and large intestine, found no ascending infection in the pancreas.

Bacterial permeability of adjacent altered viscera may be a source of infection in the pancreas. Such an extension of infection may occur primarily or secondarily after acute changes or necrosis have occurred from bile or chemical changes. The permeability of the intestine to bacteria in acute intestinal obstruction was demonstrated by McClure,[34] who found bacteria quite early in the peritoneal cavity in 45 per cent of cases of experimental obstruction of the colon and in 28 per cent of those of obstruction of the small intestine. Moynihan [35] noted in acute pancreatitis that there was usually a local dilatation and inflammation of the segment of transverse colon below the pancreas.

An abscess or peritonitis has been observed following nonperforative appendicitis, especially after catharsis (McWhorter [36]). Permeability of the intestine to bacteria has been observed under conditions such as those in typhoid fever. The production of a septic peritonitis by Bacillus welchii following the intraperitoneal injection of sterile bile and salt solution has been demonstrated by Rewbridge.[37]

Andrews and Hrdina [38] demonstrated that there was a substance in bile besides the salts that renders a change in the permeability of the bowel wall so that anaerobic bacilli may pass through and produce peritonitis with a rapid toxemia. These authors reported anaerobic

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29. Tatum: J. Biol. Chem. **27**:243, 1916.

30. Richter, H. M.: Perforating Duodenal Ulcer with Fat Necrosis, Northwestern Univ. M. School Bull., Dec., 1910.

31. Tower, L. E.: The Pathologic Physiology of Experimental Gangrenous Pancreatitis, J. A. M. A. **86**:1112 (April 10) 1926.

32. Dragstedt, L. R.: Unpublished report. Ellis, J. C., and Dragstedt, L. R.: Liver Autolysis in Vivo, Arch. Surg. **20**:8 (Jan.) 1930.

33. Patrie, Pyle and Vale: Surg., Gynec. & Obst. **24**:479, 1917.

34. McClure, R. D.: An Experimental Study of Intestinal Obstruction, J. A. M. A. **49**:1003 (Sept. 21) 1907.

35. Moynihan, Berkeley: Ann. Surg. **81**:132 (Jan.) 1925.

36. McWhorter, G. L.: Non-Perforative Appendicitis Followed by Peritonitis or Abscess, Illinois M. J. **40**:109 (Aug.) 1921.

37. Rewbridge, A. G.: The Etiological Rôle of Gas-Forming Bacilli in Experimental Bile Peritonitis, Surg., Gynec. & Obst. **52**:205 (Feb.) 1931.

38. Andrews, E., and Hrdina, L.: The Cause of Death in Liver Autolysis, Surg., Gynec. & Obst. **52**:61 (Jan.) 1931. Andrews, E.: Rewbridge, A. G., and Hrdina, L.: Causation of B. Welchii Infection in Dogs with Sterile Liver Extract and Bile Salts, Proc. Soc. Exper. Biol. & Med. **28**:136, 1930.

bacteria in the normal muscle of animals, with the production of gas gangrene by the injection of sterile bile salts and liver extract.

While pancreatitis may occur without infection, it may develop rapidly in the presence of bacteria from the normal gland or from an increased permeability of the bowel wall in the vicinity. A predisposition to extension from the intestine may be furthered by early local paralysis with ileus or by the presence of bile products in the congested pancreas.

### NONINFECTIOUS ORIGIN OF PANCREATITIS

Acute pancreatitis may occur from mechanical, traumatic, chemical, enzymatic or degenerative factors, without infection. Although most authorities support the infectious origin, especially that arising secondary to inflammation of the gallbladder, statistics show that only about one half of the cases are associated with acute cholecystitis, gallstones or evident foci of infection.

Toxic products may develop within the pancreas, or they may be regurgitated into the pancreatic ducts from the biliary tract or from the duodenum. Inactive pancreatic juice is ordinarily harmless within the pancreas, and experimental ligation of the ducts usually will not produce necrosis, although Eggers [39] obtained an acute pancreatitis when they were ligated at the height of digestion. Cutting of the pancreatic ducts with the escape of the inactivated juices into the peritoneal cavity is unaccompanied by necrosis or clinical symptoms (Senn [40] and Flexner [41]). Simple injury to the pancreas usually fails to produce necrosis, although it may liberate an activating substance. Levin [42] has shown that crushing of the gland when associated with occlusion of the blood vessels may produce characteristic hemorrhagic necrosis. Clinically, trauma of the pancreas has rather frequently been followed by acute pancreatitis and also by pseudocysts (Primrose [43]).

Lee and Adair [44] have observed fat necrosis of the breast, and Parsons [45] has shown that it may occur in any fatty tissue following an injury. Fabyan [46] described fat necrosis of the subcutaneous tissue

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39. Eggers, E. C.: Ann. Surg. **80**:193 (Aug.) 1924.

40. Senn, N.: The Surgery of the Pancreas, Am. J. M. Sc. **92**:143, 1886; **93**:121, 1887.

41. Flexner: J. Exper. Med. **8**:167, 1906.

42. Levin: J. M. Research **16**:419, 1907.

43. Primrose, A.: Surg., Gynec. & Obst. **34**:431 (April) 1922.

44. Lee, B. S., and Adair, F. E.: Traumatic Fat Necrosis of the Female Breast and Its Differentiation from Carcinoma, Ann. Surg. **80**:67 (Nov.) 1924.

45. Parsons, W. B., Jr.: Traumatic Fat Necrosis, J. A. M. A. **83**:1756 (Nov. 29) 1924.

46. Fabyan, quoted by Opie (footnote 7).

of the face in a 14 day old infant. Farr [47] produced subcutaneous fat necrosis, and expressed the opinion that it is due to a simple ischemia or liberation of lipase by the fat cells. Gottesman and Zemansky [48] expressed the belief that it may result from decomposition of the duct contents in the breast.

Bile has been known for years to be a factor in the production of acute pancreatitis, although its particular action has not been determined. Bradley and Taylor [49] have demonstrated, experimentally, that autolysis does not parallel the rapid chemical cytolysis of various parenchymatous tissues immersed in bile or its salts. They found that bile did not activate the enzymes associated with autolysis or act as a coferment, and concluded that the action must be chemical. Others have shown that bile markedly accelerates the action of the pancreatic enzymes.

Bunting and Brown [50] found that measured small amounts of bile introduced into contact with the pancreas resulted in acute hemorrhagic changes and death. Brocq and Morel [51] have shown that in order to produce an acute pancreatitis with small amounts of normal bile injected into the pancreatic duct, the injection must be made about three hours after a meal, during the height of secretion. Opie [52] found that it was necessary to inject considerable amounts of bile, which introduces the factor of trauma. Nordmann [53] found that bile alone rarely produced small areas of necrosis, but that when infection was also introduced, acute pancreatitis resulted.

Tatum found that whole bile was more toxic on parenchymatous organs, although less penetrating than the bile salts, which, also, were more toxic than the acids. Archibald found that solutions of both sodium glycocholate and sodium taurocholate, in the strength normal in human bile, produced a mild form of acute necrosis of the pancreas in cats following injection into the gallbladder. Flexner obtained necrosis by injecting bile salts, especially the taurocholate, into the pancreatic ducts.

Brocq and Binet [54] injected sodium taurocholate into the pancreatic duct, with a negative result, but obtained an acute pancreatitis with

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47. Farr, C. E.: Ischemic Fat Necrosis, Ann. Surg. **77**:513, 1923.

48. Gottesman and Zemansky: Fat Necrosis of the Breast, Ann. Surg. **85**:438 (March) 1927.

49. Bradley and Taylor: J. Biol. Chem. **29**:281, 1917.

50. Bunting and Brown: The Pathology of Intraperitoneal Bile Injections in the Rabbit, J. Exper. Med. **14**:445, 1911.

51. Brocq and Morel, quoted by Brocq, footnote 3.

52. Opie, E. L.: Diseases of the Pancreas, Philadelphia, J. B. Lippincott, 1910; Bull. Johns Hopkins Hosp. **12**:182, 1901.

53. Nordmann, O.: Arch. f. klin. Chir. **127**:600, 1923.

54. Brocq, P., and Binet, L.: Pathogénie de la pancréatite hémorrhagique, Presse méd. **31**:219 (March 7) 1923.

sodium glycocholate. They obtained no effect with biliverdine. Archibald found that sterilized mucin-free bile produced a mild pancreatitis similar to that obtained after injecting the bile salts into the gallbladder, while the injection of infected ox bile almost regularly produced a fatal pancreatitis. This infected bile showed an increased sodium taurocholate. Archibald demonstrated areas of focal necrosis in the liver within twenty minutes after the production of experimental pancreatitis. Clinically, Fischler [55] found areas of focal necrosis in the liver.

Archibald believed that there were three factors involved in acute pancreatitis: a change in the composition of the bile, an undue resistance, perhaps spasm, of the common duct sphincter and an abnormal rise of pressure in the gallbladder or the bile ducts, producing a reflux of bile into the pancreas. Bile may enter the pancreatic ducts, clinically, by two methods: (1) by obstruction of the common outlet in cases in which the bile and pancreatic ducts join, and (2) by regurgitation of the duodenal contents.

In the human being, the anatomic relation of the common bile duct and the pancreatic duct through which obstruction of the outlet may divert bile into the pancreatic duct, or vice versa, is of great importance. Opie was the first to emphasize the occurrence of acute pancreatitis by means of a gallstone obstructing the ampulla beyond the junction of these two ducts. Since then, the association of gallstones, especially in the gallbladder, has been observed frequently. Egdahl [56] found them in 42 per cent of 105 cases of acute pancreatitis. The normal incidence of gallstones in persons between 21 and 60 years of age, as noted by Mosher [57] in necropsy statistics, is 8.9 per cent.

Zuckerkandl [58] and other anatomists have found that the accessory pancreatic duct usually communicates with the major pancreatic duct by a wide opening, but that near its entrance into the duodenum the accessory duct is reduced in size and is occasionally obliterated.

Opie found in dissections in one hundred cases that the two pancreatic ducts were anastomosed in 90 per cent. The duct of Wirsung was larger in eighty-four, and the duct of Santorini in six instances. In the eighty-four cases in which the duct of Wirsung was larger, the duct of Santorini was obliterated in twenty-one. In the six cases in which the duct of Santorini was larger, both ducts were patent, while in the ten cases in which the two ducts did not anastomose, the duct of Wirsung was larger in five instances and the duct of Santorini in five.

55. Fischler: Deutsches Arch. f. klin. Med. **100**:338, 1910.

56. Egdahl: J. Exper. Med. **9**:385, 1907; Bull. Johns Hopkins Hosp. **18**:130, 1907.

57. Mosher: Bull. Johns Hopkins Hosp. **12**:253, 1901.

58. Zuckerkandl, quoted by Oser (footnote 25).

From measurements of the ampulla at the junction of the bile and pancreatic ducts, Opie believed that it was possible for a gallstone to produce a reflux of bile in 30 per cent of the cases.

Baldwin,[59] in a study of ninety cases, found that the ducts opened separately into the duodenum in 25.8 per cent, while in 74.2 per cent, there was a common ampulla. Mann and Giordano[60] believed from their observations that the reflux of bile was anatomically possible in only 4.5 per cent. Cameron and Noble[61] were able to impact a carefully selected calculus in the ampulla of Vater, and to produce a reflux of fluid from the bile ducts into the pancreatic duct in 65 per cent of one hundred cases.

Obstruction at the ampulla in the absence of gallstones may be due to a spasm of the sphincter of Oddi (Archibald), congestion, inflammatory swelling, and obstruction by mucus and by intestinal parasites. The resistance of the common duct sphincter varies considerably in animals and also in the human being, as evidenced by a difference in tension of the gallbladder at operation. Archibald[62] found the resistance of the sphincter to be from 500 to 650 mm. of water in animals, while Mann[63] rarely found it over from 100 to 150 mm. I[64] observed it to average from 100 to 250 mm., although there was considerable variation beyond these limits. The resistance may be temporarily and partially reduced by the application of a 25 per cent solution of magnesium sulphate. Archibald produced a spasm of the sphincter by the introduction of a 3 to 5 per cent solution of hydrochloric acid into the duodenum, followed by acute pancreatitis, although this usually required a slightly increased pressure in the biliary system.

In a human pancreatic fistula, Villaret and Justin-Besancon[65] found that magnesium sulphate in the jejunum produced the appearance of bile without pancreatic secretion, while hydrochloric acid produced the opposite effect. Local duodenal congestion and catarrhal inflammation of the papilla may cause stasis and reflux of bile into the pancreas.

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59. Baldwin: The Pancreatic Ducts in Man Together with a Study of the Microscopical Structure of the Minor Duodenal Papilla, Anat. Rec. **5**:197, 1911.

60. Mann, F. C., and Giordano, A. S.: Bile Factor in Pancreatitis, Arch. Surg. **6**:1 (Jan.) 1923.

61. Cameron, A. L., and Noble, J. F.: Reflux of Bile up the Duct of Wirsung Caused by an Impacted Biliary Calculus, J. A. M. A. **82**:1410 (May 3) 1924.

62. Archibald, E.: A General Consideration of Pancreatitis, Internat. Clin. **2**:1, 1918.

63. Mann, F. C.: A Study of the Tonicity of the Sphincter at the Duodenal End of the Common Bile Duct, J. Lab. & Clin. Med. **5**:106, 1919.

64. McWhorter, G. L.: The Surgical Significance of the Common Duct Sphincter, Surg., Gynec. & Obst. **32**:124 (Feb.) 1921.

65. Villaret and Justin-Besancon: Arch. d. mal. de l'app. digestif **15**:751 (Oct.) 1925.

Balo and Ballon [66] reported three cases of acute pancreatitis with obstruction of the papilla due to venous congestion resulting from a decompensated heart; others have noted these findings due to gastroduodenitis, following dietary indiscretion or accompanying catarrhal jaundice.

That a reflux of pancreatic juice may occur into the biliary tract is evidenced by the finding of trypsin in sterile bile in a case of gangrenous cholecystitis by Schonbauer.[67] Experimentally, he was able to produce a gangrenous cholecystitis with trypsin in sterile bile together with obstruction of the outlet. This occurrence has been corroborated experimentally by the recent work of Wolfer.[6]

The presence of the almost constant anastomosis observed between the two pancreatic ducts in the presence of patency of both ducts and the junction of the major duct with the bile duct above the sphincter would seem to predispose to a reflux of bile into the pancreas. Under these conditions, increased biliary pressure would tend to produce a reflux of bile into the pancreas regardless of the amount of pancreatic secretion due to the release of pressure by way of the accessory duct. In the absence of this anastomosis between the two pancreatic ducts and in the presence of obstruction at the ampulla during the height of pancreatic secretion, it is possible that pancreatic juice might be regurgitated up the biliary ducts and into the gallbladder.

It has been observed after cholecystectomy that either the bile ducts may dilate with a continent sphincter at the outlet (Rost [68]), or the sphincter of Oddi may dilate with incontinence (Judd). There may be a disturbed nerve reflex leading to relaxation of the common duct sphincter, as previously suggested (McWhorter, 1921) and recently favored by Puestow [69] because of his observing a rapid loss of sphincter tonus after cholecystectomy. Unless such a reflex loss of sphincter tone occurs after cholecystectomy, there must occur an initial increased biliary pressure until either the bile ducts dilate to compensate for the gallbladder or the common duct sphincter becomes dilated and incontinent.

A primary increased biliary pressure occurring after a cholecystectomy would seem to predispose to an acute pancreatitis. In chronic pancreatitis, Judd believes that cholecystectomy is curative, while Archibald advocates prolonged common duct drainage. Acute pancreatitis with cyst formation occurred after cholecystectomy in a case of Ballin and Saltzstein.[70] However, one patient (Miller [1]) died of

66. Balo, J., and Ballon, H. C.: Effects of Retention of Pancreatic Secretion, Surg., Gynec. & Obst. **48**:1 (Jan.) 1929.

67. Schonbauer: Arch. f. klin. Chir. **130**:427 (Aug. 29) 1924.

68. Rost: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **26**:711, 1913.

69. Puestow, C. B.: Proc. Staff Meet., Mayo Clin. **6**:23 (Jan. 14) 1931.

70. Ballin, M., and Saltzstein, H. C.: Pancreatic Cyst Following Cholecystectomy, J. A. M. A. **76**:1484 (May 21) 1921.

acute pancreatitis a few days after drainage of the gallbladder was performed with removal of stones, although no changes were noted in the pancreas at the time of operation.

Acute pancreatitis with death resulted from the reflux of bile into the pancreatic duct owing to the swelling of the papilla from instrumental dilatation at operation in a case of Rost.[71] He formerly dilated the papilla of Vater and sutured the common duct after a choledochotomy.

Regurgitation of duodenal contents into the pancreatic ducts, with or without infection, may produce necrosis of the pancreas. Experimentally, Polya[72] produced typical pancreatitis by injections of small amounts of duodenal contents. There are a number of factors in the duodenum that may produce pancreatitis, including bile, gastric juice, enterokinase, intestinal secretions and bacteria.

In support of the duodenal origin of acute pancreatitis may be mentioned the large proportion of clinical cases in which the bile tract was not inflamed, although the condition of the sphincter was not often determined. The actual method of duodenal origin has rarely been demonstrated clinically. Opie and Barling have been unable to force duodenal contents into the bile or pancreatic ducts in human specimens. It is possible that a regurgitation might occur into the pancreatic duct in the presence of an acute or chronic (Leveuf[73]) dilatation of the duodenum or with a relaxed or dilated sphincter. This may be favored by antiperistalsis (Hlava).

Intestinal parasites may carry toxic products or infection into the pancreatic ducts and obstruct them, producing acute pancreatitis (Rigby[74] and Novis[75]). Carnot produced acute pancreatitis by passing a thread into the pancreatic duct and irritating the duodenum with croton oil. Hess[76] produced it by fastening a funnel-shaped cannula in the duct and obstructing the duodenum below it. He believed that olive oil in the duodenum favored the production of pancreatitis. Brocq produced the condition experimentally by complete obstruction of the duodenum following a gastro-enterostomy. Seidel[77] also produced pancreatitis by stasis of the duodenum.

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71. Rost: Zentralbl. f. Chir. **54**:20 (Jan. 1) 1927.

72. Polya: Berl. klin. Wchnschr. **43**:1562, 1921.

73. Leveuf, J.: Rev. de chir., Paris **58**:616, 1920; quoted by Brocq (footnote 3).

74. Rigby, H. M.: Acute Hemorrhagic Pancreatitis: Round Worms in Pancreatic Duct, Brit. J. Surg. **10**:421, 1923.

75. Novis: Partial Obstruction of the Pancreatic Duct by Round Worms, Brit. J. Surg. **10**:421, 1923.

76. Hess: München. med. Wchnschr. **52**:644, 1905.

77. Seidel, quoted by Brocq (footnote 3).

Clinical cases have been observed by Gerhardi [78] and Konig-Werth [79] with stenosis of the duodenum. The duodenal origin of pancreatitis seems probable in a number of instances in which the common bile and pancreatic ducts were found to empty separately (Opie and Barling). Johnstone [80] alone reported four cases. In some, necrosis was limited to the region drained by one pancreatic duct. Bassett [81] reported a case with necrosis limited to the region of the duct of Santorini, in which the outlet terminated in an inflamed diverticulum. There was a mucous plug in the ampulla below the junction of the bile and major pancreatic ducts, with a free communication between the two pancreatic ducts.

Opie suggested that while the delicate valves in the diverticulum of Vater may normally prevent regurgitation, in 10 per cent of the cases the duct of Santorini is the chief outlet, and its orifices may be less able to prevent regurgitation. He reported such a case with complete necrosis along the unusually large duct of Santorini, the orifice of which admitted a probe 2 mm. in diameter, but there were only slight changes along the small duct of Wirsung.

Brocq expressed the belief that the greater predominance of hemorrhage in some cases of acute pancreatitis and of fat necrosis in others is due to a different origin. In the former, it was due to the duodenal contents, with a particularly increased trypsin activity and digestion of the blood vessel walls, while in the latter it was due to bile, with a resulting increased action of the lipase on the fats.

Acute pancreatitis may be produced by the injection of diphtheria toxin (Carnot and Brocq), acid gastric juice (Hlava), alkalis (Flexner), calcium chloride, formaldehyde and leukocytes without bacteria, although normal serum injected into the duct under strong pressure did not produce it (Brocq). In the absence of a chemically toxic bile in the pancreas, the production of a cytokinase or the activation of trypsin may be obtained in some other way. That diastase and other ferments are usually present in acute pancreatitis is evidenced by their early, frequent occurrence in increased amount in the blood and urine and their absence in other abdominal conditions (Unger and Heuss [82]).

Trauma from increased pressure in the pancreatic ducts may be of considerable importance in acute pancreatitis. Degenerative changes, such as atheroma of the blood vessels, resulting in spontaneous hemorrhage, those associated with tumors and cysts and those resulting from the toxins of bacteria and infectious diseases may produce pancreatitis. A combination of two or more predisposing factors may be necessary to produce acute pancreatitis in many instances.

78. Gerhardi, quoted by Hess (footnote 76).
79. Konig-Werth, quoted by Hess (footnote 76).
80. Johnstone: Colorado Med. **4**:93, 1907.
81. Bassett: Tr. Chicago Path. Soc. **7**:83, 1907.
82. Unger and Heuss: Zentralbl. f. Chir. **54**:769 (March 26) 1927.

Fat necrosis is a frequent but not necessary occurrence in acute pancreatitis (Balser [83]), and Ponfick [84] early directed attention to fat necrosis in the fat of the omentum and peritoneum. Moynihan observed fat necrosis in the fat of the abdominal wall in acute pancreatitis. Fitz has shown that fat necrosis is rare in the suppurative type. Fat necrosis is often widely disseminated, and has been seen in the pericardium. Oser believed that these changes are not a result of contact with pancreatic secretion. However, in experimental pancreatitis, fat necrosis has been found just as widespread by Opie. Wells [85] has suggested the rôle of the lymphatics in this diffusion. Local congestion and the extravasation of ferments from the blood might be considered as a possible source. Several cases of fat necrosis without gross lesions of the pancreas are reported. Opie expressed the belief that some of these were due to obstruction of the pancreatic duct by a gallstone. Wood [86] suggested that the fat-splitting ferment, steapsinogen, may be activated in the pancreas by some constituent of the bile. Flexner demonstrated a fat-splitting enzyme in the necrotic foci.

The pathologic changes are the result of the splitting of fat into soluble glycerin and fatty acids, which are deposited as needle-like crystals within the necrotic cells and later unite with calcium, forming globular masses. The small areas of necrosis are surrounded later by a zone of round cell infiltration. Wells found that a moderate amount of fat necrosis might be absorbed in a week after its production. He found that pancreatin injected into the peritoneal cavity produced fat necrosis.

While experimental section of the pancreatic duct does not produce acute pancreatitis, I have observed in one instance several widely scattered areas of fat necrosis on the pancreas. Flexner showed that sterile but activated pancreatic juice may cause pancreatitis. Activation of trypsin is believed to result from some substance formed in the autolyzed pancreas (Lattes [87]). Wells observed that trypsin and lipase were inactive after autolysis, although trypsin was still present.

Fitz found that autolysis destroyed the fat ferment but not the tryptic ferment, which may explain the absence of fat necrosis in extensive necrotic pancreatitis. Injury to the pancreas may produce a cytokinase, and there may also be a leukokinase and a bacteriokinase (Brocq and Binet). Rewbridge has shown that bile free in the

83. Balser: Ueber Fettnekrose, Virchows Arch. f. path. Anat. **90**:520, 1882.

84. Ponfick: Virchows Arch. f. path. Anat. **56**:541, 1872.

85. Wells, H. G.: J. M. Research **9**:70, 1903; Chemical Pathology, Philadelphia, W. B. Saunders Company.

86. Wood, W. Quarry: The Etiology of Acute Pancreatitis, Edinburgh M. J. **30**:201 (May) 1923.

87. Lattes: Pathologica **4**:577, 1912, quoted by Goodpasture and Clark: Bull. Johns Hopkins Hosp. **18**:2, 1919.

peritoneal cavity may produce fat necrosis, and that this is due to the action of the bile salts. He suggested that the pancreatic enzymes are liberated by permeability changes produced by the local action of the bile on the pancreas.

There are several theories regarding the cause of death in acute pancreatitis in which the following conditions are considered: nervous shock, anaphylaxis, toxemia and local or generalized infection.

The theory that a nervous shock is produced is based on the adjacent sympathetic plexus. Linder [88] believed that early acute prostration may result from pressure of an enlarged pancreas against the celiac plexus, and that later a toxemia occurs. Archibald and Kaufman [89] believed that irritation of the plexus may produce paralysis of the intestine with neurogenic shock. The resemblance to an anaphylactic shock is advocated by Silvestri,[90] who suggested that sensitization is produced by previous mild attacks of pancreatitis. Toxemia undoubtedly may develop rapidly from local infection in the pancreas or peritoneum.

Toxemia is usually believed to be due to the split products of pancreatic autolysis (Guleke [91]) or digestion by trypsin (Whipple and Goodpasture [92] and Tower). This toxemia is evidenced by an increased proteose index, and is not due directly to an increase in trypsin in the blood, although an increase in antiferment favors recovery (Peterson, Jobling and Eggstein [93]).

Goodpasture and Clark [94] have found a toxic constituent that may be gradually destroyed by autolysis in fresh pancreas, before activation of trypsinogen. However, if trypsinogen is activated by the duodenal juices, immediate death may result, as observed by Lombroso [95] and Roger and Garnier.[96] Archibald and Kaufman explained the belief that the particular toxin in acute pancreatitis was probably a histamine. The peritoneal exudate was formerly considered toxic (Guleke); however, Cook and Whipple [97] and Whipple and Goodpasture injected this

88. Linder, W.: Acute Pancreatitis, J. A. M. A. **69**:718 (Sept. 1) 1917.

89. Archibald, E. A., and Kaufman, M., in Lewis, Dean: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1929.

90. Silvestri, T.: 1922, quoted by Brocq (footnote 3).

91. Guleke, N.: Beitr. z. klin. Chir. **48**:127, 1906. Gross, O., and Guleke, N.: Die Erkrankungen der Melz der Leber, der Gallenwege und des Pankreas, Enzyklopaedie der klinischen Medizen, Berlin, Julius Springer, 1924, p. 115.

92. Whipple and Goodpasture: Surg., Gynec. & Obst. **17**:541 (Nov.) 1913.

93. Peterson, Jobling and Eggstein: J. Exper. Med. **23**:491, 1916.

94. Goodpasture and Clark: A Study of a Toxic Substance of the Pancreas, Bull. Johns Hopkins Hosp. **18**:2, 1919.

95. Lombroso, quoted by Wood (footnote 86).

96. Roger and Garnier: Compt. rend. Soc. de biol. **64**:885, 1908.

97. Cook and Whipple: J. Exper. Med. **28**:223 (Aug.) 1918.

fluid into the peritoneum and veins of animals without any ill effects. They concluded that the toxemia was nonspecific and resulted from the breaking up of protein and cell autolysis. Egdahl found that autolyzed pancreatic extracts depressed blood pressure, and that the toxic effects were greatest when the protein had been completely digested.

Sweet,[98] Doberauer [99] and Guleke removed a part of the pancreas aseptically from one animal and placed it in the peritoneal cavity of another; death invariably occurred in twenty-four hours. However, bacteria may be present in the normal pancreas of animals (L. Dragstedt).

Whipple [100] has called attention to a postoperative asthenia due to acute and chronic lesions of the pancreas, followed by a high mortality.

Fat necrosis is probably not the toxic factor in acute pancreatitis, since it may occur alone without toxic general symptoms, and it is frequently more extensive in the older and less toxic cases.

The following study is based on an analysis of sixty-four cases of acute idiopathic pancreatitis.

## ETIOLOGY AND PREDISPOSING FACTORS

The age in all sixty-four cases varied from 19 to 70 years, but was chiefly between 30 and 60 years. The average age was 43.3 years. Comparing the average ages in the four pathologic types or grades of pancreatitis, the youngest age, 39 years, occurred in the highly fatal hemorrhagic type II; the next higher age, 42 years, occurred in the subacute type I; the age in the suppurative type IV averaged 47 years, and the highest average age, 51 years, was in the gangrenous type III. This comparison shows the mortality rates to be higher in the youngest, the hemorrhagic type, and in the oldest, the gangrenous type, than in the others (table 1).

There were an equal number of both men and women, which is at variance with the reports of most authors that acute pancreatitis is much more frequent in men.

In comparing the sex incidence in the different pathologic types of pancreatitis, it was found that almost an equal number of each sex had the subacute and the hemorrhagic types. More women than men had the gangrenous type, but nine men and three women had the suppurative type. This tends to confirm the theory that infection is more commonly associated with pancreatitis in the male.

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98. Sweet: Internat. Clin. **4**:293, 1915.

99. Doberauer: Beitr. z. klin. Chir. **48**:127, 1906.

100. Whipple, A. O.: Pancreatic Asthenia as a Postoperative Complication in Patients with Lesions of the Pancreas, Ann. Surg. **78**:176 (Aug.) 1924.

Among the twenty-six patients having gallstones, there were eleven men, with six deaths, a mortality of 54 per cent, and fifteen women, with eight deaths, a mortality of 53 per cent. However, gallstones occurred in only 30 per cent of the men who died, as compared to an occurrence of 53 per cent in the women who died. Considering the

TABLE 1.—*Etiology, Predisposing Factors and Treatment in Pancreatitis*

| | Number of Cases | Percentage of Frequency | Percentage of Mortality |
|---|---|---|---|
| Idiopathic acute pancreatitis | 64 | .. | 54.7 |
| Type I, acute edematous pancreatitis | 18 | 28 | 28 |
| Type II, acute hemorrhagic pancreatitis | 27 | 42 | 70 |
| Type III, acute necrotic or gangrenous pancreatitis | 7 | 10 | 70 |
| Type IV, acute suppurative pancreatitis | 12 | 20 | 50 |
| Men in total of 64 cases | 32 | 50 | 62 |
| Women in total of 64 cases | 32 | 50 | 47 |
| Obesity in total of 64 cases | 17 | 26 | 85 |
| Alcoholism in total of 64 cases | 7 | 11 | 70 |
| History of typhoid fever | 5 | 8 | 60 |
| Numerous childbirths | 7 | 11 | 42 |
| Emaciation | 5 | 8 | 64 |
| Jaundice | 9 | 14 | 55 |
| No previous abdominal symptoms | 17 | 26 | 59 |
| Sugar in the urine | 8 | 12 | 62 |
| Some type of diseased gallbladder, total | 35 | 54.5 | 52 |
| Gallstones, total | 26 | 40 | 53 |
| Gallstones in 32 men | 11 | 34 | 54 |
| Gallstones in 32 women | 15 | 47 | 53 |
| Acutely inflamed gallbladder | 14 | 22 | 50 |
| Gallstones with chronic inflammation but without acute gallbladder changes | 18 | 28 | 55 |
| Chronic inflamed gallbladder without stones | 3 | 5 | 33 |
| Acutely inflamed gallbladder without stones | 6 | 9 | 50 |
| Gallstones with acute inflammation of the gallbladder | 8 | 12 | 50 |
| Chronic inflammation of the gallbladder, with and without stones, total | 21 | 33 | 57 |
| No acute or chronic gallbladder inflammation, total | 29 | 45 | 58.8 |
| (a) Gallbladder distended | 8 | 12 | 37 |
| (b) Gallbladder noted as definitely normal | 16 | 25 | 56 |
| (c) Gallbladder not mentiond | 4 | 6 | 50 |
| Treatment: | | | |
| (a) No operation | 6 | 9 | 100 |
| (b) Operation; exploration without drainage | 7 | 11 | 57 |
| (c) Operation with four chief types of drainage | 51 | 80 | 49 |
| 1. Drainage only of peritoneal cavity | 13 | 20 | 77 |
| 2. Drainage of pancreas alone, with and without abscess | 4 | 6 | None |
| 3. Drainage of gallbladder or common duct | 25 | 39 | 56 |
| 4. Drainage of gallbladder and pancreas | 9 | 14 | 11 |

much higher mortality rate in men (62 per cent) than in women (47 per cent), this observation would indicate that other factors than gallstones may cause and influence the mortality in acute pancreatitis.

Although gangrenous pancreatitis developed more commonly in women and the suppurative type more commonly in men, the mortality was lower in the latter type, so that suppuration was probably not the chief factor in increasing the mortality. It is probable that non-suppurative and anaerobic infection were present in some of the other cases, especially in the gangrenous group.

The mortality rates in the cases with acute inflammation of the gallbladder but without stones were practically equal in both sexes, but the series was small.

*Childbirth.*—In two patients, the onset of pancreatitis occurred shortly after childbirth, four days in Percy's patient and three weeks in Gatewood's. In the latter, there had been previous frequent attacks, with acute cholecystitis also found at operation. In both instances, there were gallstones, and both patients recovered. Seven patients had borne numerous children, but some records were incomplete.

There was a history of typhoid fever in five cases (three women and two men). Two of these patients had type I pancreatitis, two had type III and one had type II. Other previous diseases noted were: arthritis deformans, twice; pneumonia, once; malaria, once; pyorrhea and otitis media, once, and syphilis, once. Several patients had been operated on previously—appendectomy, twice; gallstones with removal of the gallbladder and drainage, once; a pelvic operation, once; an abdominal abscess, once, and a perforated duodenal ulcer two weeks previous to the attack, once.

There were seventeen, or 26 per cent of the patients, who were definitely obese and five who were emaciated. Practically all of the remaining patients were stated to be well nourished. The cases of suppurative pancreatitis, type IV, showed the greatest number of obese patients and the cases of gangrenous pancreatitis, type III, the fewest.

There were seven patients, or 11 per cent, who gave a history of persistent alcoholism. A few others were occasional drinkers. The alcoholic patients nearly all had hemorrhagic pancreatitis, type II. In two instances the onset occurred the morning after a drinking bout.

*Exciting Factors.*—Infection in the pancreas or its surroundings was noted in a number of instances, but few bacteriologic studies were recorded. The rare occurrence of acute or chronic inflammation, except in the biliary tract and the pancreas, in both the cases that came to necropsy and those in which operation was performed, suggests an interrelation of their infection. Acute inflammation of the gallbladder was described in fourteen, or 22 per cent, of the sixty-four cases. Gallstones were found with chronic inflammation in eighteen, or 28 per cent, and chronic inflammation without stones in three cases, or 5 per cent. There was a total of some type of acute or chronic inflammation or stones in the gallbladder in thirty-five cases, or 55 per cent of the total.

Seventeen of the twenty-nine patients in whom the gallbladder was considered to have no acute or chronic inflammation gave a history of previous symptoms in the upper part of the abdomen. However, one had a duodenal ulcer.

No symptoms or evidence of any foci of infection was noted as a source of the acute pancreatitis in these cases, and practically all patients were in excellent health at the onset. Since sixteen had previous symptoms in the epigastrium without any other pathologic process than pancreatitis, it is possible that they suffered from mild attacks of pancreatitis, although attacks of cholecystitis may have occurred leaving no gross changes. If these previous symptoms were due to attacks of pancreatitis, they were probably limited to the pancreas and due to local conditions, such as diversion of bile, extension of infection along the lymphatics, bile ducts or blood vessels, or the activation of latent infection.

In eleven other cases in which the patients had a normal gallbladder and had had no previous symptoms, infection from the biliary tract seems unlikely as a cause for the acute pancreatitis. The presence of acute inflammation of the gallbladder in only 22 per cent of the entire series also speaks for this as a secondary condition. The diversion of bile into the pancreatic ducts may produce acute pancreatitis, without primary infection, although infection may subsequently develop within the gland or extend from the duodenum. In the presence of gallbladder infection one may infer that the infection spread to the pancreas or vice versa. When infection occurs in the gallbladder, it may produce chemical changes in the bile that render it toxic and may activate the pancreatic juices when regurgitated into the pancreas.

The evidence speaks against infection as the exciting factor in the first three types of pancreatitis and indicates that when infection occurred, it was a complication.

Infection may ascend the ducts in the presence of inflammatory obstruction at the ampulla or rapidly permeate the intestinal wall, following distention and stasis, especially with necrosis or gangrene of the pancreas. It is possible that hematogenous emboli may have occurred in one instance (Miller), although local infection is the more probable.

In favor of regurgitation of bile as a cause of pancreatitis is a case that came to necropsy in which the pancreatic duct was found bile-stained, and several cases in which obstruction was present at the ampulla, including two with an impacted gallstone. Obstruction may have been overlooked in other instances, or only temporary obstruction may have occurred, such as obstruction due to a stone, muscle spasm, inspissated mucus, congestion or inflammation.

In cases in which diversion of bile at the ampulla was anatomically impossible, a regurgitation of activating juices or extension of infection from the duodenum may have occurred.

PATHOLOGY

A division of acute pancreatitis into four pathologic types seemed advisable for this detailed study. Although these types represent different degrees of severity of the process, the classification conforms to the condition found at the time of examination and represents the particular stage at that time rather than the final degree of the pathologic process. To a large extent the four types represent a varying degree of severity and rate of extension of the process. It is quite probable that different factors may predominate in the pathogenesis of each type, and certainly the diagnosis, prognosis and treatment may be more correctly determined by such a working classification.

Type I includes eighteen cases of acute or subacute pancreatitis in which no hemorrhage was seen or recorded and in which the pancreas was usually enlarged, edematous and hard. In two cases it was described as nodular and in two as soft, while in three instances it was described as simply edematous.

Type II includes twenty-seven cases in which hemorrhages were recorded as present in the pancreas in the absence of gross gangrene or suppuration. The pancreas was also usually enlarged and hard or edematous.

Type III includes seven cases with gross necrosis or gangrene of the pancreas in the absence of suppuration.

Type IV includes twelve cases in which there was suppuration or a definite abscess in the pancreas. In four cases there was also necrosis.

Microscopic examinations were made in three cases at necropsy. There was extensive necrosis in one and leukocytic infiltration in one; in the other there was no normal pancreatic tissue, only areas of degeneration separated by loose connective tissue with infiltration of small round cells. There was one case of syphilis of the liver in type III. Areas of fat necrosis were examined in five cases. They showed small areas of necrosis surrounded by an infiltrated zone of small round cells and leukocytes in the fat tissue.

There was a tumor or enlargement in the epigastrium in thirty-four cases, although it was palpated clinically in only fifteen instances. In three other cases in which a tumor was diagnosed clinically, it was not found at operation. The frequency of a mass was about the same in the various types of pancreatitis. The mass was found to be an enlarged pancreas in twenty-one cases, a thickened omentum in four, an abscess in four, a retroperitoneal hemorrhage in two, and in two (Percy-Nadeau and J. Smith) a pseudocyst with suppuration in the pancreas (McWhorter [101]).

101. McWhorter, G. L.: Cysts of the Pancreas, Arch. Surg. **11**:619 (Oct.) 1925.

Fluid was present in the abdomen in thirty-eight cases, or 60 per cent, and it was often quite abundant. The frequency was about the same in all types, although somewhat greater in type I. The type of fluid was described as bloody fourteen times, yellow twice, greenish or bile-stained four times, chocolate-colored three times, slate-colored once, turbid twice, and containing fat globules once. Bloody fluid was more frequent in the hemorrhagic type, and bile-stained in the suppurative type. In the patients having fluid, the mortality was 66 per cent.

Fat necrosis was recorded as present in fifty-five, or 83 per cent, of the sixty-four cases. In two cases in which it was not recorded, there was suppuration.

Gallstones were the most frequent associated pathologic condition. They were found either at operation or at necropsy in twenty-six, or 40 per cent, of the patients, of whom fourteen died. Gallstones were found in the common duct in five patients. In two who died a stone was found at necropsy impacted in the ampulla of Vater. There was obstruction, with jaundice due to inflammation of the common duct, but without stones, in two other cases. In one, the common duct was distorted and narrowed.

Acute inflammation of the gallbladder was present in fourteen, or 22 per cent, of the patients, of whom seven died. There were gallstones present in eight of these, with four deaths. Chronic inflammation of the gallbladder was noted in twenty-one cases, with eleven deaths. This condition was fairly equally distributed among the four types of pancreatitis.

In twenty-five cases, or 39 per cent, in which the gallbladder was not recorded as inflamed, there were fifteen deaths, or a mortality of 60 per cent. The gallbladder was distended in eight of these, with three deaths. In sixteen, the gallbladder was recorded as perfectly normal, with nine deaths, or 56 per cent.

Thick black bile was reported in four cases, with three deaths. If four cases in which the gallbladder was not mentioned, with two deaths, are considered as showing no disease of the gallbladder, there is a total of twenty-nine cases having no evidence of involvement of the gallbladder, with a mortality of 58.8 per cent.

Among the fifteen patients examined post mortem, there was involvement of other viscera than the pancreas and the biliary tracts, including the gallbladder, in only nine. Infection was the cause of most of the associated pathologic involvement, usually due to a local extension and occasionally to pyemia. There was acute suppurative pleuritis, once; bilateral fibrous pleuritis, twice; subphrenic abscess, once; abscess of the kidney with bronchopneumonia, once, and phlegmonous gastritis with multiple embolic abscesses of the liver, once.

There was chronic perihepatitis, gastritis and splenitis with pleuritis, once; chronic interstitial hepatitis, once; syphilitic hepatitis with gummas, once, and local perforating ulceration into the colon, once. Degenerative and late changes were usually associated with infection. In the liver, fatty changes were observed in four cases. In the kidney, chronic nephritis was noted twice, cloudy swelling twice and fatty changes once. In the spleen, thrombosis of the splenic vein and hyperplasia were each noted in one case. In the heart, fatty changes were observed in one case.

Acute parotitis occurred in three patients after operation, and all died. In one, there was local pancreatic sepsis, and in another systemic sepsis for three days. Digestion of the wound was much less common than is usually believed. It occurred in three suppurative cases. In one case, the wound gaped widely owing to digestion of the sutures, and did not heal before death on the sixteenth day. In another, there was marked digestion about a fistulous opening for several weeks. In the remaining case, the digestive action was slight. Apparently, there may be considerable drainage of pancreatic juice, which at times may have little effect on the wound. This would indicate that factors which may activate the pancreatic juice and produce a necrosis are transient.

The cause of death was believed to be toxemia in twenty patients, of whom five were not operated on. The next most common cause was local sepsis, thirteen cases: two of these patients were not operated on. One patient died of pyemia and toxemia, and the remaining patient had a postoperative hemorrhage. In the first three types of pancreatitis, death from sepsis occurred in about the same proportion of the fatalities, while in the suppurative type IV, all six deaths were due to local sepsis.

### SYMPTOMS

There was a history of previous attacks of acute abdominal pain in twenty-four cases, or 37 per cent. In at least two of these, the attacks were similar to the pains during acute pancreatitis. Previous attacks of pain of a milder but similar character were noted in four other cases. Two patients had been operated on previously for a condition diagnosed as chronic recurrent appendicitis.

Previous attacks of chronic distress in the stomach or abdomen occurred over varying periods of time and degree in fourteen cases, or 22 per cent. Types I and III pancreatitis were found more frequently in the patients having had previous chronic distress, and types II and IV in those giving a history of previous attacks of pain.

There were forty-two patients, or 65 per cent, exclusive of the two with chronic appendicitis, who gave a history of previous attacks of pain or abdominal distress. Among these were twenty-three in

whom gallstones or acute cholecystitis were found present during the attack of acute pancreatitis.

There were seventeen of the forty-two patients having previous symptoms of pain or distress in whom no gallstones or inflammation were noted either at operation or, in four of them, at necropsy. The occurrence of previous abdominal symptoms in practically 40 per cent of those with a normal gallbladder is suggestive of previous mild attacks of pancreatitis. There may be factors causing attacks of pain that could not be determined, such as a past cholecystitis, spasm or temporary obstruction of the common bile duct by a gallstone, without noticeable changes to be seen at operation.

There were ten patients who gave no history of previous attacks of pain or abdominal distress in whom either gallstones or acute inflammation of the gallbladder, or both, were found. Eight of these had gallstones.

The onset of the pancreatitis was acute, with no previous symptoms, in eight, or 30 per cent, of the twenty-six patients having gallstones, but acute cholecystitis was found in only four of these.

There was no history of previous abdominal symptoms in seventeen cases, or 26 per cent, with ten deaths, or 59 per cent. Four were cases of type I pancreatitis, with three deaths, or 75 per cent, which is significant, since the average mortality was 28 per cent in this type. Eight were cases of type II pancreatitis, with five deaths. There was one fatal type III case. There were four cases of type IV pancreatitis, with only one death. This would seem to favor the theory that previous mild attacks occur which develop immunity, and that infection is not a necessary factor, but may develop as a serious complication if the patient does not die of the toxemia.

Pain was present in all of the cases, and usually its onset was sudden, severe, prostrating and persistent. However, in one case of type IV pancreatitis, it was very slight. In two cases of a type II condition it was intermittent. In two cases of type III pancreatitis it was constant, with severe exacerbations. The location of the pain was stated to be in the epigastrium in twenty-five cases, over the region of the gallbladder in ten, at the umbilicus in two and in the right lower quadrant in three cases. In one case (Phemister), the pain was located in the right groin and thigh, simulating neuritis. There was radiation of the pain to the right shoulder twice, to the left shoulder four times and to the back once.

Rigidity was usually definite but not boardlike. It varied somewhat, and in two cases it was absent on examination. The rigidity was generalized over the abdomen in thirty cases, localized to the epigastrium in five and to the right upper quadrant in nine.

Tenderness was usually a leading complaint, and was not absent in any case. It was general in twelve, localized in the epigastrium in twelve and in the right upper quadrant in twelve cases. The locality was not stated in eleven cases.

Vomiting was usually persistent. In one instance, the vomitus was bloody. This symptom was absent in six patients and occurred only at the onset in two others. In three of the six patients in whom vomiting was absent, there was no nausea. Belching was an occasional symptom.

Fever was frequently absent or only slight during the early course. Chills were not noted. There were nine patients (14 per cent) with no recorded fever at any time before operation. Three of these had a subnormal temperature. There were four whose temperatures did not rise over 100 F. The maximum temperature in thirty cases in which it was recorded before operation averaged 102 F. The temperature varied from an average of 98 to 102 F., and often remained normal a large part of the day. Only three patients had a temperature over 103 F., and two of these had a temperature of 105 F.

The average maximum pulse rate recorded before operation in forty-two patients was 110. In two instances, the maximum pulse rate was 60 before operation; in twenty-three instances, it was over 120. In only nine patients was the rate under 100.

A bluish discoloration of the upper abdominal wall, followed later by edema, was given considerable diagnostic significance by Kanavel, and was noted in two patients.

A mass in the epigastrium was noted clinically in eighteen patients, but in three none was found at operation. There were nine in whom no tumor was palpated, and yet a definite mass was found at operation. In some instances, the inability to palpate a fairly large swelling was due to marked tympanites, which was especially frequent in the critically ill hemorrhagic type. In five other cases, an indefinite resistance was felt in the epigastrium, but no mass was found at operation.

Jaundice was observed in nine patients with five deaths. Two patients had pancreatitis type I; two, type II; two, type III, and three, type IV. There were two patients without jaundice in whose urine bile was present, and both recovered.

The urine contained sugar in eight cases, with five deaths. Albumin and casts were recorded in eighteen cases, with nine deaths. Blood was present in three fatal cases of type II. The urine was recorded as normal in ten cases, with five deaths.

The white blood count recorded in thirty-five cases averaged 20,000. Thirteen of the patients recovered with an average count of 17,000, while twenty-two who died had an average of 21,000 leukocytes. In type I, nine patients, most of whom recovered, averaged 17,000 leuko-

cytes. In type II, fourteen patients averaged 21,000, of whom eleven died. The highest count was 42,000 in a fatal case, while one patient with a count of 32,000 recovered. There were two fatal type II cases, with a count of 7,800 and 11,900, and four fatal type III cases, with an average count of 16,700. There were eight type IV cases, with an average count of 23,800, with five deaths.

The stools in one case were grayish white, containing bile but no blood. In another case, in which the patient recovered, blood was present. The bacteriologic reports in two cases (Schrager) showed a colon bacillus cultured from the gallbladder contents. In one (Percy-Nadeau) the discharge from the wound was sterile. In another (McWhorter) cultures from the very thick gallbladder bile of a critically ill patient were sterile.

Roentgenograms of the stomach in one case were negative, except for a slight six hour residue.

### PROGNOSIS

There were thirty-five deaths in the sixty-four cases, or 54 per cent. In comparing the ages of the patients in the different pathologic types of pancreatitis it was found that the youngest average occurred in hemorrhagic type II, and the oldest in gangrenous type III. The mortality rate was the same in both, but it was higher than in the two other types. Apparently, age is not a decisive factor in the prognosis. Twenty, or 62 per cent, of the men died, and only fifteen, or 47 per cent, of the women died.

Among patients with predisposing factors, the highest mortality rate, or 85 per cent, was that of obese patients, while 90 per cent was the rate for patients with a history of alcoholism. There was a mortality of 64 per cent of those who were emaciated, and 60 per cent of those with a history of typhoid fever. For the patients who gave no history of any previous abdominal symptoms or of any serious systemic diseases, the mortality rate was 5 per cent above the average. Among the nine patients who were jaundiced, the mortality rate was 55 per cent. The development of jaundice was apparently not an especially unfavorable symptom, except in the suppurative type of pancreatitis, in which it was very serious. There was a lowered mortality, 42 per cent, among seven patients who had borne several children.

The mortality rates in cases complicated by obesity, alcoholism, previous typhoid or numerous pregnancies were compared for the different types of pancreatitis. In subacute type I, the mortality rates in all these cases, except those complicated by obesity, were lower than the average. In the hemorrhagic and gangrenous types, the mortality rate was much higher when any of the complicating factors was present, while in the suppurative type of pancreatitis, the mortality rates dropped

to below the average. The mortality curve for all cases in which any of these factors was present tends to parallel the average mortality in all types, but it was higher in the hemorrhagic and gangrenous types of pancreatitis.

The patients who recovered usually had a slightly lower average white blood count, although there were exceptions, two patients who died, with a normal count. The mortality of the eight cases in which sugar was present in the urine was 62 per cent. There were three cases of pancreatitis, type I, in which sugar was present, with one death. In the hemorrhagic type of pancreatitis, sugar was found in four cases, but in one it was present only after operation. Three of these were fatal cases. The remaining case occurred in the suppurative type and was fatal. There is apparently an increased mortality in cases of pancreatitis in which sugar occurs in the urine except in the milder cases. Diabetes developed in one patient three years later, although sugar was not found during the pancreatitis. A completely normal urine was apparently of little value in prognosis, although albumin and casts usually were present in the more severe cases. Among several hundred diabetic patients, Dunn [102] noted only two having a history of acute pancreatitis.

The mortality rate was studied in relation to the duration of time of the pancreatitis from the onset to the time of operation. Twenty-three patients with a recent acute onset underwent emergency operations, although the actual duration of the disease was not recorded. Nine died and fourteen recovered, but only one case had a type I pancreatitis. Eight patients were operated on less than one day from the onset of the disease. Six of these died; five had the hemorrhagic type of pancreatitis. Considering the thirty-one cases as of recent onset before operation, the mortality rate was 48 per cent, slightly less than the average.

There were fourteen cases in which over one day and less than one week had elapsed before operation, the average time being from two to four days. Nine patients died, or 64 per cent. Most of these had the hemorrhagic type of pancreatitis, with a mortality of 83 per cent. There were three cases in which the onset occurred two months previous to operation, and all the patients died. Of the six patients with pancreatitis on whom operation was not performed, all died following an acute onset.

From a further study of the deaths in the different types of pancreatitis, it is evident that they were more dependent on the extent of the pathologic involvement than on the time elapsing from onset to operation.

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102. Dunn; Vatcher and Woodwork: Diabetes as a Sequel to Acute Pancreatitis, Lancet **1**:595 (March 20) 1926.

The lowest mortality rate was in a group of nine cases in which operation was performed at about the end of two weeks after the onset of the condition, there were only two deaths, or 22 per cent. Since these nine patients were nearly all desperately sick, it seemed worth while to study their cases in detail. There was suppuration in four cases with one death, and the other three patients would undoubtedly have died if drainage had not been instituted. In three patients with hemorrhagic pancreatitis, one having jaundice died, while in the others, who recovered, an acutely inflamed gallbladder was drained. In two of these cases of type I pancreatitis exploration was done and the wound closed without drainage, with recovery. Among the seven survivors were five women and two men, while the two deaths occurred in men. Analyzing all cases, the mortality rate was found to be lower in all four types of pancreatitis following an early operation, unless the patients were moribund at the time of operation.

The average age of all survivors in the sixty-four cases was 40 years, and that of the patients who died, 34 years. The average age of the men and the women was the same. Six patients died before they could be operated on. The length of time after operation until death occurred was compared in twenty-nine patients. Eleven deaths occurred within a day after the operation, and ten within from two to four days. The majority of the remaining eight deaths occurred within from two to three weeks, although, exceptionally, death occurred over a month after operation. These cases were divided fairly equally among the four types of pancreatitis; in the suppurative type, there were no deaths following the third day after operation.

In reviewing the mortality rates of the varying intervals before and after operation, and analyzing the different types of pancreatitis, it is evident that operation is urgently indicated in the presence of pancreatic suppuration or acute cholecystitis. Operation is also indicated for patients seriously sick at the end of the second week. It is only among patients with the nonsuppurative types of pancreatitis, including the hemorrhagic type, requiring operation at this time that there is a lowered mortality. One may conclude that operation is usually indicated as an emergency in all types of pancreatitis, at the end of the second week if there is no definite improvement.

In the absence of suppuration or gangrene in the pancreas, the inference might be drawn that mere drainage of the pancreatic capsule is of little value. If one could correctly diagnose the absence of infection in the pancreas or biliary tract, it might seem unnecessary to operate merely to drain the pancreas until complications developed, and then operation should be performed preferably about two weeks after the onset. However, it is evident that one should operate in all acute cases of pancreatitis, if possible, as an emergency procedure because of the

frequent presence of gallstones, acute cholecystitis, necrosis and infection or suppuration in the pancreas. Since it is only in the cases of nonsuppurative pancreatitis in which operation has been performed that the mortality rate is low, one may conclude that drainage of the pancreas may prevent secondary anaerobic infection and suppurative changes or at least limit their extension.

The relation of gallbladder disease to the mortality is of considerable importance, because the presence of gallstones was the most frequently associated pathologic condition with acute pancreatitis. The mortality in cases with gallstones was slightly less than in those without them, except when the stones were impacted in the ampulla of Vater. Gallstones were present in twenty-six cases, with fourteen deaths, a mortality of 53 per cent. They occurred in the common duct five times, and in the two patients who died a stone was impacted in the ampulla of Vater. Comparison of the mortality rates in the four pathologic types of pancreatitis with gallstones (table 2) shows that they parallel the mortality rates in cases without stones; that is, the rate is higher in the hemorrhagic and gangrenous types.

Acute inflammation of the gallbladder was present with gallstones in eight cases, with four deaths, while in eighteen cases with gallstones but without acute inflammation, there were ten deaths, or 55 per cent.

Acute inflammation of the gallbladder was present in fourteen of the sixty-four cases, with seven deaths. The mortality was 50 per cent in eight cases with stones and in the six cases without them. While both gallstones and acute cholecystitis may predispose to pancreatitis, at first glance they apparently do not affect the average mortality rate. However, on comparing the mortality rates of the cases with acute cholecystitis in the different types of pancreatitis (table 2), it was found that the mortality was lower than the average in the hemorrhagic type of pancreatitis, and higher, or 100 per cent, in the gangrenous and suppurative types. The series is small, but it definitely indicates the seriousness of acute infection of the gallbladder in both gangrenous and suppurative pancreatitis.

Chronic inflammation of the gallbladder was recorded in twenty-one cases, with eleven deaths, a mortality of 57 per cent. Eighteen of these patients had gallstones, with a mortality of 55 per cent, and three did not have them, with a mortality of 33 per cent. The occurrence of these cases in the four different types of pancreatitis was about equal, although the mortality was unusually high, 88 per cent, in the hemorrhagic type.

The gallbladder was considered as practically normal in twenty-five cases, with fifteen deaths, or 60 per cent. In sixteen of these cases, the gallbladder was recorded as entirely normal, with nine deaths, or 56 per cent; although more of the cases occurred in the hemorrhagic

type, the mortality rates corresponded fairly well to the average. In all except two the course was found to have been fulminating in character and nearly all of these patients were operated on either the second or third day or death occurred rapidly after the onset. This would seem to indicate that the acute pancreatitis was primary, and that inflammation of the gallbladder more frequently developed in the less fulminating cases.

In four cases in which the gallbladder was not examined, there were two deaths. In eight cases the gallbladder was distended, with only three deaths; however, more of these cases occurred in type I pancreatitis. In comparing the mortality in all cases with acute inflammation of the gallbladder and those with a normal gallbladder, the mortality was found to be higher in the latter. The lowest average mortality rate of the four pathologic types of pancreatitis in the sixty-

TABLE 2.—*Mortality in the Four Types of Pancreatitis* *

| | I Acute Edematous Pancreatitis, per Cent | II Hemorrhagic Pancreatitis, per Cent | III Necrotic or Gangrenous Pancreatitis, per Cent | IV Suppurative Pancreatitis, per Cent |
|---|---|---|---|---|
| Average mortality | 28 | 70 | 70 | 50 |
| Mortality in 26 cases with gallstones | 20 | 66 | 66 | 33 |
| Mortality in 14 cases with acute cholecystitis | 33 | 37 | 100 | 100 |
| Mortality in 16 cases with an entirely normal gallbladder | 12 | 75 | 75 | 37 |

* The mortality rates vary directly with the severity of the pathologic process in the pancreas and complicating conditions of the gallbladder.

four cases was 28 per cent in type I, which might be considered the best criterion by which to judge the prognosis as affected by gallbladder disease. On analyzing the cases in type I, 33 per cent of the patients with acute inflammation of the gallbladder died, 20 per cent having gallstones died, and only 12 per cent died in whom the gallbladder was normal (table 2).

In the suppurative type of pancreatitis the average mortality rate was 50 per cent, but in cases complicated by acute cholecystitis, it was 100 per cent. The mortality was also increased in the gangrenous type, complicated by inflammation of the gallbladder, but there was a lowered mortality in the hemorrhagic type. It is evident that the inflammation of the gallbladder did not develop at the onset in many fulminating cases, but when present it usually increased the mortality.

In the suppurative type of pancreatitis, the most serious complication next to cholecystitis was jaundice, which was present in three of the six patients who died. Aside from the cases in which jaundice was present, the mortality rate was almost as low as in type I. Appar-

ently with the development of a suppurative pancreatitis, one may expect a fairly low mortality rate if operation is performed and drainage instituted, unless jaundice is present.

### DIAGNOSIS

The symptoms of pancreatitis are fairly characteristic, but resemble those of several other serious abdominal conditions. In subacute type I pancreatitis, two cases were correctly diagnosed. The diagnosis of an acutely inflamed gallbladder condition was made and found present in four other cases. Mistaken diagnoses were made as follows: appendicitis, once; carcinoma of the stomach, twice, and various other conditions, seven times. In two instances, no clinical diagnosis was made.

In the hemorrhagic type, three cases were correctly diagnosed. Wrong diagnoses were made as follows: acute cholecystitis, seven cases; a perforating gallbladder, two; a perforating gastric ulcer, six; acute appendicitis, two, and carcinoma of the pancreas, one. No diagnosis was made in six cases.

In the gangrenous type of pancreatitis a correct diagnosis was made once. An acute condition of the gallbladder was diagnosed in four cases, but it was not associated in two of them. A wrong diagnosis of a perforating gastric ulcer was made once. No diagnosis was made in one case.

In the suppurative type of pancreatitis the diagnosis was made correctly twice. The diagnosis was partly correct in a case of associated perforating duodenal ulcer once and of a perforating gallbladder once. No diagnosis was made in four cases, and an incorrect diagnosis of an acute condition of the gallbladder was made in three cases.

In all cases of acute pancreatitis a correct diagnosis was made only eight times, or in 12 per cent. In eight other cases a correct diagnosis of an acute condition of the gallbladder or of a perforated viscus was made, but the pancreatitis was not suspected. The diagnosis was wrong in forty-eight cases, or 75 per cent. The most frequent mistaken diagnoses were: acutely inflamed gallbladder, perforating gastric or duodenal ulcer, acute appendicitis, carcinoma of the stomach or pancreas and acute peritonitis.

### TREATMENT

In the sixty-four cases reviewed, no operation was performed on six patients, all of whom died. An exploration was done in seven cases, mostly type I pancreatitis, with an immediate closure without drainage; four of the patients died, or 57 per cent. Of the remaining fifty-one patients who were operated on, twenty-five, or 49 per cent, died.

Four chief procedures were followed at operation in the cases in which the wound was drained: (1) simple drainage of the peritoneal

cavity, chiefly in types I and II pancreatitis, with three recoveries and ten deaths, or a mortality of 77 per cent; (2) drainage of the pancreas or of an abscess within it in four cases in the suppurative type IV, with recovery in every case; (3) drainage of the gallbladder, which occasionally included the common duct, done in twenty-five cases, eleven patients recovering and fourteen dying, a mortality of 56 per cent, and (4) drainage of the gallbladder together with drainage of the pancreas or its capsule in nine cases, eight patients recovering, with a mortality of only 11 per cent.

This analysis would indicate that some drainage of the pancreas or its capsule should be introduced in all except perhaps the simple edematous type of acute pancreatitis. Drainage of the gallbladder alone does not always check a pancreatitis; therefore it is safer to institute prophylactic drainage of the pancreas in all cases, since it may prevent anaerobic infection or abscess formation. Biliary drainage is indicated in most cases with an associated jaundice and particularly with acute or chronic inflammation of the gallbladder or with gallstones.

If there is an abscess or infection in the pancreas, with an absence of obstruction or acute inflammation of the biliary tract, drainage of the pancreas alone should be sufficient. In the prophylaxis of acute pancreatitis one should remove all foci of infection, including the gallbladder in most instances of biliary tract disease, together with any gallstones (McWhorter [103]). Other important points are the avoidance of alcoholism and treatment for obesity.

Efforts have been made by Brocq to check the flow of pancreatic juice in acute pancreatitis by the use of atropine and also by neutralizing the acid chyme and thus to prevent the formation of secretin.

Immunization of animals has been attempted on the theory that death is due to a toxemia as a result of the action of trypsin. Ohno [104] has immunized animals by injecting activated trypsin into the peritoneal cavity and has obtained a highly immune serum, which has been used in four patients without ill effects. Schonbach [105] and Schonbauer have produced active immunization and immune serum experimentally.

While von Bergmann and Guleke [106] and Joseph and Pringsheim [107] were able actively to immunize against pancreatic necrosis

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103. McWhorter, G. L.: Preventive Surgery of the Pancreas and Bile Ducts, Illinois M. J. **47**:128 (Feb.) 1925.

104. Ohno, R.: Mitt. a. d. med. Fakult. d. k. Univ. Kynshu Univ. Fukusha (Japan) **7**:31, 1923; quoted by Brocq (footnote 3).

105. Schonbach, quoted by Brocq (footnote 3).

106. von Bergmann and Guleke: München. med. Wchnschr. **57**:1673, 1910.

107. Joseph and Pringsheim, quoted by Gross and Guleke (footnote 91, second reference).

through increased doses of trypsin and to lessen its intoxication, they were not able to obtain a serum from these animals for satisfactory passive immunity.

Spontaneous recovery may frequently occur in subacute pancreatitis (Moynihan and Mikkelson [108]). Resection of the necrotic portion of the pancreas has been done where the necrosis is limited to the distal portion (Hofmann [109] and Butler and Delprat [110]), but it is rarely indicated because of the difficulty in technic and the danger of hemorrhage and shock.

Körte reviewed 103 cases of acute pancreatitis, with a mortality of 60 per cent. He observed that more patients recovered who were operated on early in the first week, and he advised early operation.

Brocq reviewed 340 cases. Among 235 patients with acute hemorrhagic pancreatitis, 116 were operated on before 1910, with a mortality of 78 per cent, and 119 since 1910, with a mortality of 68 per cent. He believed that the mortality was lowered in many instances by supplementing drainage of the pancreas with drainage of the biliary tract.

In seventy cases of suppurative pancreatitis he noted a mortality of 51 per cent, and in thirty-five cases with subacute or edematous pancreatitis a mortality of 23 per cent. Drainage of the biliary tract in addition to drainage of the pancreas seemed to favor recovery, except in the suppurative form, in which drainage was associated with a higher mortality. There were seventy-seven patients with various types of pancreatitis on whom no operation was performed, and all died.

Early operative relief for biliary tension was emphasized by Archibald and Kaufman, who recommended biliary drainage even in subacute pancreatitis and in the absence of gallbladder inflammation. In addition, they advised drainage of the pancreas by a gauze drain, but warned against tearing the living tissue.

The performance of a cholecystectomy without biliary drainage is contraindicated because of the danger of subsequent increased biliary pressure and of prolonging the operation. In the mild cases, or exceptionally, cholecystectomy may be indicated. One is rarely justified in exploring for or attempting to remove a common duct stone, especially in the severe cases; one should merely institute biliary drainage. If exploration of the common duct is indicated, one should note whether the outlet is occluded or dilated. If the outlet is dilated, prolonged biliary drainage will not be indicated. In case of partial or total obstruction, due to congestion at the outlet, dilatation of the sphincter should

108. Mikkelson, O.: Hospitalstid. **81**:132, 1925, quoted by Eliason and North: Surg., Gynec. & Obst. **51**:183 (Aug.) 1930.

109. Hofmann, A.: Arch. f. klin. Chir. **114**:1041, 1920.

110. Butler and Delprat: Acute Hemorrhagic Pancreatitis, Surg., Gynec. & Obst. **42**:379, 1926.

not be attempted, owing to the danger of increased swelling. If it is possible one may insert a small catheter through the common duct into the duodenum with a separate tube for the proximal drainage of bile. This will produce a further dilatation of the sphincter (McWhorter, 1921 and 1925) and will also permit the instillation of fluids into the duodenum (McArthur [111]). Under such conditions a further reflux of bile into the pancreatic duct is prevented and drainage of pancreatic secretion may occur around the tube into the duodenum.

Most surgeons strongly advocate early operation in all except the mild or the moribund cases of acute pancreatitis, although Mikkelson defers operation until symptoms of diffuse peritonitis or abscess formation occur.

It is evident that the value of operative treatment depends on the type of pathologic condition present, but in most instances this can be determined only at operation. As a rule, the more severe the local and associated pathologic involvement, the more valuable will be properly executed operative intervention.

## SUMMARY

The division of acute idiopathic pancreatitis into four pathologic types is of value in the study of this highly fatal condition. Obese patients and those with a history of persistent alcoholism have a greatly increased mortality.

Gross infection of the pancreas was found to be present more frequently in men. Some type of inflammation of the gallbladder or stones was present in 55 per cent of all cases, with little variation from the average mortality. Gallstones were present in fewer men than in women, although when present the mortality rate was identical. However, only 30 per cent of the men who died had gallstones, as compared to 53 per cent of the women. The higher mortality rate, 62 per cent, in men than in women, 47 per cent, indicates the presence of other factors than gallstones affecting the mortality. Acute inflammation of the gallbladder was present in only 22 per cent of all the cases. Evidences of obstruction of the common duct were found in a few cases. In two an impacted stone was found in the ampulla at necropsy.

There was little evidence of a regional or distant focus of infection existing before the onset of pancreatitis in any of the cases. In the majority of the cases of pancreatitis, pathologic changes were not found outside of the pancreas and the bile tracts. Gallstones, in addition to obstructing the ampulla, possibly may predispose to pancreatitis even when in the gallbladder, by disturbing the physiology of the biliary tract pressure and sphincter action. It is probable that regurgitation

111. McArthur, L. L.: Journal-Lancet **36**:723 (Dec. 15) 1916.

of bile into the pancreatic duct occurs rather frequently, and that there are contributing factors that modify the bile or otherwise contribute in producing acute pancreatitis.

Acute inflammation of the gallbladder may be a predisposing factor, but probably is more frequently a complication of pancreatitis. In many cases of acute pancreatitis pyogenic bacteria are found, but anaerobic bacteria are undoubtedly early invaders, especially when necrosis is present. There was a definitely lower mortality in the cases in which operation was performed immediately as compared to those in which operation was performed from the second to the fourth day after the onset of the disease. The mortality was also lower in a few cases in which it was performed at about the end of the second week.

When suppuration of the pancreas or inflammation of the gallbladder was present, the mortality was lower in cases in which early operation with appropriate drainage was performed. However, there remained an unusually high mortality in cases in which both an acute inflammation of the gallbladder and necrosis or suppuration of the pancreas were present.

Since all of the patients not operated on died, it is evident that early diagnosis is important, and should be followed by an emergency operation, unless the patients are moribund or definitely improving. Drainage of the pancreas should be established in all cases, except perhaps in the mild edematous type in which prophylaxis against infection may seem unnecessary.

Exploration of the biliary tract followed by drainage should be done in practically all cases, particularly in the presence of inflammation, gallstones or jaundice. In cases in which evident infection is localized in the pancreas, particularly after the first few days, drainage should usually be limited to the pancreas.

In a further effort to reduce the mortality, one must attempt to reduce the incidence of pancreatitis. This should include the prevention of and treatment for obesity, gallstones and foci of infection. Active or passive immunity may offer some hope for the future. Prophylaxis by the early removal of gallstones and well chosen operations on the gallbladder for acute and chronic cholecystitis may prevent hepatic, pancreatic and other serious complications.

# A REVIEW OF UROLOGIC SURGERY

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## KIDNEY

*Anomalies.*—Papin, Bernasconi and Bernard [1] reviewed the 27 cases of true supernumerary kidney reported in the literature. The relative frequency of the malformation could not be discovered, but it must be extremely rare. The supernumerary organ was on the right side in 12 cases, on the left in 14 cases and in the middle in 1 case. Nine occurred in females; 16 in males; in 2 cases the sex was not noted.

In some cases the kidney was only subjacent; in others, it was located at the iliac artery or the psoas muscle. The form was seldom indicated; in 1 case it was lobulated; in another, bean-shaped with convex anterior aspect. In the case of Bernasconi and Bernard the lower kidney was of normal shape, and the upper, supernumerary organ was concave on its lower surface, which fitted the rounded top of the lower kidney, the latter being lodged within it. The anomalous kidney was sound, and the normal kidney was diseased, having a stone in the ureter. The size of the kidney varied. In 2 cases the lower kidney was larger than the upper. In 10 cases there were only two ureteral orifices into the bladder, suggesting that the ureters were fused. In 2 cases the tract of the upper ureter was unusual; it dug a furrow in the supernumerary kidney before becoming fused with its ureter. In 1 instance the ureter of the supernumerary kidney turned upward and

1. Papin, Bernasconi and Bernard: Contribution à l'étude du rein surnuméraire, Arch. d. mal. d. reins **6**:1 (June) 1931.

entered the descending ureter of the upper kidney at the level of the superior pole of the lower kidney. In another case the two kidneys and their pelves had a single ureter, which passed from the upper to the lower and then to the bladder. In 11 cases there was complete duplication of the ureter. Two orifices opened into the bladder in 8 cases; the orifice was into the vagina in 2 cases and into the vulva in 1 case. In 1 case there were four ureteral openings into the bladder.

In 21 cases there were symptoms during life; in 6 cases the lesion was discovered at necropsy. There were three classifications of the cases: (1) a healthy supernumerary kidney, accompanied by pain or small concomitant malformations due to its abnormal position; (2) a diseased supernumerary anomaly, and (3) the association of some additional anomaly causing special symptoms. Certain cases were characterized by pain and an abdominal tumor. In 1 case the supernumerary organ was on the left side, but the pain was on the right. Usually calculi were present; these were sometimes in the normal kidney or its ureter.

Nephrectomy was performed in 16 of the cases. In 3 cases the transperitoneal route was used; in 8 the lumbar; in 3 cases two kidneys were removed by the lumbar route; in 1 case nephrostomy was done on one kidney, then two kidneys were removed by lumbar incision; in 2 cases nephrotomy was done for calculi.

The type of double kidney in which one kidney is invaginated into the other, designated by the authors as supernumerary kidney with impaction, is omitted from this consideration. The only cases included are those in which there are three separate parenchymatous masses of the kidney.

Jeck [2] stated that in 16,735 necropsies at Bellevue Hospital during the last twenty-six years, twenty-six horseshoe kidneys were found, one in every 643 cadavers. Necropsy statistics indicate that the life span of persons with horseshoe kidneys is relatively short.

The urographic characteristics on which a diagnosis of horseshoe kidney is based are mainly: renal pelves closer to the median line and lower than normally placed kidneys; shortening of one or both ureters; a tendency of the calices to point downward or toward the vertebrae, and calices of bizarre shapes, absence of calices or calices overlapping the pelvis.

Preoperative diagnosis of horseshoe kidney makes it possible to perform more easily and with greater facility whatever operation may be necessary than when the condition is encountered accidentally. Most surgeons with experience in operating on horseshoe kidneys prefer the extraperitoneal route to the transperitoneal. With an adequate incision and the extraperitoneal approach there is less likelihood of infecting the

2. Jeck, H. S.: Horseshoe Kidney with Especial Reference to Surgical Technic; Report of Cases, J. A. M. A. **98**:603 (Feb. 20) 1932.

peritoneum, especially when dealing with tuberculosis, pyonephrosis or infected hydronephrosis, and of reducing the probability of infecting the peritoneum in cases of pyelotomy or nephrotomy or in heminephrectomy, if the stump of the isthmus should subsequently secret urine.

In considering heminephrectomy, the operation most frequently necessitated by the pathologic conditions found in horseshoe kidneys, the function and size of the other half of the kidney should be determined; also whether the other kidney has its own separate ureter, whether there are accessory arteries and veins, whether the kidney which is to remain has ample blood supply, and the size and composition of the isthmus. In ligating the renal pedicle, care should be taken not to tie the vessel or vessels which supply the only branch to the half of the kidney which is to remain. In 13 per cent of 60 cases studied at necropsy, Robinson found a single arterial trunk for the isthmus which divided, one branch supplying the right renal mass and the other the left.

Since 1918, in approximately 400 operations on the kidney in the Bellevue urologic service, there were 4 cases of horseshoe kidney. The condition was recognized preoperatively in 2 cases. In 3 of the cases, heminephrectomy was performed without any particular difficulty. The isthmus was small and chiefly fibrous; accessory blood vessels were also present, but were easily recognized. In the fourth case small bilateral calculi were removed from the right side by pyelotomy and nephrotomy; several days later secondary heminephrectomy became necessary because of hemorrhage.

Lazarus[3] stated that the anomaly of horseshoe kidney occurs in about 0.1 per cent of normal persons. There are no characteristic symptoms of horseshoe kidney; when they do occur they are caused by some associated pathologic lesion, to which they are more susceptible than normally formed kidneys. The diagnosis of this condition is usually made at operation or at necropsy. A flat renal roentgenogram will generally lead to the suspicion of this anomaly by showing the proximity of the kidney silhouette to the vertebral column, by the obliteration of the psoas margins in part or in their entirety and by the failure to visualize one or the other of the renal poles. The diagnosis may be corroborated by pyelography, showing the bizarre pelves and calices, usually pointing anteriorly and approximated to the median line, and shortening of the ureters.

Heminephrectomy is the preferred treatment for an extensive suppurative lesion, tumor or tuberculosis involving half of a horseshoe kidney. Other lesions are treated in the same manner as are similar diseases in normally formed kidneys.

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3. Lazarus, J. A.: Horseshoe Kidney: A Report of Five Cases, J. Urol. **27:** 471 (April) 1932.

[COMPILERS' NOTE.—The frequency of horseshoe kidney, as well as that of the associated lesions, has given rise to a definite clinical syndrome, recently described by Gutierrez. In a recent series of cases he has shown that the clinical diagnosis of horseshoe kidney can usually be obtained before operation by means of present-day proficiency in urography. The diagnosis was conclusively made in 19 of 25 cases studied by Gutierrez [4] in which a urologic examination was made. Jeck has correctly emphasized the fact that the extraperitoneal route of surgical approach is the safer, and that the transperitoneal method of exploration employed in the days before urography must not be used on account of the possibility of peritoneal infection.

In some cases there is a definite indication for symphysiotomy, or the division of the isthmus of the horseshoe mass, followed by nephropexy. This insures better drainage of the kidney and helps to eliminate the symptoms associated with fusion, which are usually due to the median line situation of the organ, even though a lesion is not present.]

*Tumors.*—Hager [5] stated that the syndrome of tumor, pain and hematuria occurs late in the course of renal tumors. He pointed out that the early symptoms are vague, and urged repeated examination in such cases. Repetition of all the tests of renal function with retrograde and intravenous pyelography should yield a diagnosis in early suspicious cases. The significance of renal displacements and irregularities in contour in the roentgenogram is emphasized. If all signs fail and a tumor is still suspected, an exploratory operation should be done. Seventeen cases of renal tumor are reported, 2 of which occurred in children. Pyrexia was a prominent symptom in 4 of the 15 adults and in both children. Three of the adults had metastasis. The diagnosis was confirmed in every case by operation.

[COMPILERS' NOTE.—The incidence of pyrexia in these cases is rather unusual. As the author pointed out, an occasional high temperature is at times striking and a significant symptom. It occurs in approximately 10 per cent of reported cases. In some cases the fever is suggestive of metastasis and may be associated with severe, widespread bodily pains. In a case reported in which marked pyrexia was present before removal of the kidney, the reappearance of a high temperature was the first symptom indicating recurrence and metastasis.]

Darmady [6] stated that squamous cell carcinoma is the rarest type of malignant growth of the renal pelvis. Up to 1924 only 60 cases of

4. Gutierrez, Robert: The Clinical Management of Horseshoe Kidney, Am. J. Surg. **14**:657 (Dec.) 1931; **15**:132 (Jan.); **15**:345 (Feb.) 1932.

5. Hager, Ilse: Beitrag zur Diagnostik der Nierentumoren, Berl. Klinik **38**: 1, 1931; abstr., Am. J. Cancer **15**:3023 (Oct.) 1931.

6. Darmady, E. M.: Squamous-Cell Carcinoma of the Renal Pelvis, St. Barth. Hosp. J. **38**:118 (March) 1931.

this lesion were reported in the literature; 6 cases have been reported since then, making a total of 66. Numerous cases have been ascribed to renal calculi of long standing, but Miller and Herbst have shown that of 54 cases in which an examination was made, only 10 can be attributed to renal stone. Cumming stated that the normal transitional epithelium can become replaced by a many-layered coating of stratified squamous epithelium with superficial keratinization. This condition of leukoplakia is associated with infection, stone and hydronephrosis.

Darmady reported a case of squamous cell carcinoma of the renal pelvis in which an operation was performed in 1930. Hydronephrosis had been present twenty-eight years before. The size, weight and striking lamination of a calculus removed at operation indicated that the latter had also been present for a number of years.

Stux [7] reported a case of teratoma of the right kidney of an infant aged 9 months. The growth had been noticed in the right side of the abdomen one month previously and had increased rapidly in size until it reached from the ribs to the iliac crest and mesially to the median line. It was smooth, oval, not tender and fluctuant. Repeated urinalysis showed traces of albumin and the constant presence of a few erythrocytes. At operation the mass was found to be cystic, and could be removed only after several of the cysts had been punctured. The child died two days later of pneumonia. At necropsy, the left kidney did not contain a tumor.

Pathologic examination revealed that the tumor arose from the upper and inner portion of the right kidney. In a collapsed state it measured 11 by 8 by 7 cm. and weighed 368 Gm. The entire mass was well encapsulated; its surface was slightly lobulated. On section numerous cysts of various sizes were found, separated by a small amount of compact cellular tissue. Microscopically the cysts were lined with high cylindric or cuboidal epithelium. The supporting connective tissue was infiltrated with small round cells which showed numerous phases of mitosis. The diagnosis of an embryonal mixed tumor of the kidney was made.

[COMPILERS' NOTE.—Most tumors of the kidneys of children occur during the first two years of life. The pelvis of the kidney is generally not involved; consequently urinary symptoms and pain are rare. These neoplasms grow rapidly; the increase in size is generally due to intrarenal hemorrhage. The average length of life after the onset of symptoms is about eight months; following nephrectomy it is from sixteen to twenty months. Death is almost certain if operative procedures are

7. Stux, Herbert: Zur Frage über die malignen Nierentumoren im frühen Kindesalter, Arch. f. Kinderh. **92**:128 (Dec. 19) 1931; abstr., Am. J. Cancer **15**:3025 (Oct.) 1931.

not carried out. Nephrectomy often prolongs life and offers the only chance for improvement. Earlier writers all agree on the unusually high mortality rate.

Stux designated his case as that of teratoma of the kidney. These growths usually have the same characteristic histologic structure. The predominating structures are groups of incompletely formed glands surrounded by masses of irregularly disposed cells. They may contain striated muscle, squamous cell nests and, more rarely, areas of bone and cartilage.]

*Stone.*—Schultheis [8] stated that the origin of urinary calculi, especially that of renal stones, is still unknown. The following theories have been assumed: (1) disposition of the particular organism to formation of stone, either a uric acid or phosphate diathesis, or other factors such as geographic, alimentary or exogenous influences, and (2) a changed excretory threshold, such as disturbance of the intermediary cell product exchange of the kidney which causes a change in the colloidal equilibrium of the urine and results in a precipitation of crystalloid elements.

The pathologic histology does not show any primary changes in either the renal parenchyma or the lower part of the urinary tract by which the formation of stone can be explained. The histologic changes in kidneys containing stones are secondary to the calculi.

Schultheis is of the opinion that calculi originate in the pelvis and when found in the calices, have emigrated there. A kidney with a stone has a lowered resistance and may be infected by either the lymphogenous, hematogenous or urogenous route. A movable stone may lead to pressure changes between Bowman's capsule and the glomerulus. When a stone migrates to the pelvis, there may be obstruction leading to intermittent hydronephrosis or pyonephrosis. Clinically, stones are either aseptic or infected. In the former case the condition is usually acute, with stasis and pressure changes, whereas in the latter there is destruction of the organ, depending on the virulence of the organism.

Gottstein classified the pathologic anatomy of kidneys containing stone as follows: (1) the normal appearing kidney, (2) the atrophic kidney, (3) the so-called perirenal fat kidney (replacement lipomatosis) and (4) the calculous hydronephrotic and pyonephrotic kidney.

From a study of 26 cases of renal stone the following conclusions were drawn: There is usually pyelitis of varying degrees, depending on the size of the stone, and limited renal function and associated infection. In the aseptic cases there may be glomerulotubular nephritis with more atrophic tendencies, whereas in infected cases there is more or less

8. Schultheis, Theodor: Histologische Untersuchungen an Steinnieren, Ztschr. f. urol. Chir. **31**:193 (March) 1931.

inflammation present, the interstitial tissue being partly atrophic, edematous and hypertrophic. Occasionally there are individual cases with notable changes in vessels, such as sclerosis of the arteries. There is the small inflammatory group characterized by an increase in the fibrous and fatty capsules.

[COMPILERS' NOTE.—In spite of an enormous volume of literature and an extensive amount of laboratory investigation with the experimental production of calculi in animals, we have as yet a very incomplete understanding of the pathologic changes incident to the formation of stone. As brought out by Schultheis, altered anatomic changes in the kidneys are not consistent or of especial significance in clarifying the problem. Inflammatory reactions, atrophy and the features associated with stasis comprise the details of the picture. Certainly the presence of stone lowers renal resistance and renders the affected kidney liable to the pathologic changes associated with chronic and acute infection, sclerotic processes and, at times, neoplasia.]

Braasch [9] stated that repeated recurrence of renal stone is not common, and if it does occur, etiologic factors are present other than those causing the usual single or occasional calculi. In a review of the postoperative results in more than 1,000 cases of nephrolithiasis at the Mayo Clinic, he found that stone recurred in approximately 10 per cent of the cases. There was recurrence subsequent to a second operation in only a few cases, approximately 2 per cent.

The exact factors involved in the etiology of lithiasis are still unknown. Opinions are divided as to whether the condition is caused by abnormal metabolism or infection, while there is reason to believe that both factors may be involved. It is generally accepted that abnormal metabolism is the usual cause of recurrent stones composed of uric acid, cystine and xanthine, as shown by the fact that uric acid stones cease to form when the patient is placed on a purine-free diet. The repeated formation of stone may also be due to infection, such as occurs with urea-splitting bacteria. Bacteriologic studies at the Mayo clinic by Hager and Magath have shown that infection with Proteus ammoniae is often the direct etiologic factor in the formation of phosphatic stones. That some anatomic factor causing retention in a calix, the renal pelvis or the ureter may be a primary factor permitting such infection is also possible. Most recurring stones of this type are composed largely of calcium phosphate. Renal stones composed of fibrin are exceedingly rare, particularly in cases in which stones form repeatedly.

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9. Braasch, W. F.: Recurring Renal Lithiasis, Proc. Staff Meet., Mayo Clin. **7**:169 (March 23) 1932.

Braasch reported a case of frequently recurring stones composed chiefly of fibrin in both kidneys and apparently caused by renal infection with Proteus ammoniae. In an effort to overcome the infection due to this bacteria, continuous drainage of the renal pelvis was established for three days, and the pelvis was lavaged with a strong solution of silver nitrate without materially affecting the bacterial growth. An unsatisfactory attempt was made to dissolve the reforming calculus by means of lavaging the pelvis with a 10 per cent solution of karoid, an enzyme employed in destroying dead organic material. On the supposition that the stone now present is composed of calcium phosphate, the renal pelvis has recently been washed with phosphoric acid, in a solution of 1 and 2 per cent. Although this has not affected the stone so far, it has undoubtedly been a factor in reducing the infection. Microscopic examination of specimens from the right kidney does not reveal pus or bacteria. The patient's general condition is now apparently normal; the voided urine, which is not abnormal in amount, contains a small amount of pus and many Proteus ammoniae and is less alkaline than before.

[COMPILERS' NOTE.—The solution of urinary calculus in situ by means of chemicals applied through a ureteral catheter or by ingestion of drugs has met with practically no success. Turpentine once was in vogue in such efforts, but its virtues were probably mythical. Crowell has reported solution of cystine stones by the application of alkalies, and Randall has applied phosphoric acid in the case of phosphatic stones. Even in the test tube phosphatic calculi require concentrations of acids for their solution which are hardly applicable to the pelvic mucosa. Fujamaki has described the disappearance of calculi in rats when calculosis has been produced by the deletion of vitamin A from the diet. After feeding for a certain length of time food with a high content of vitamin A, such experimental calculi disappeared. Perhaps these observations will in time lead to a new form of treatment in lithiasis. At present recurrent lithiasis presents a problem. With the realization of our inadequacy, we attempt to correct by attempting to relieve stasis and infection in the manner which the author has outlined.]

*Tuberculosis.*—Ivarsson [10] reported 192 cases of renal tuberculosis, in 156 of which nephrectomy was performed. Subsequent data were obtained in 190 of the cases, in 155 of which nephrectomy was performed.

Extrarenal, chronic tuberculosis occurred in 55.8 per cent of the cases in which nephrectomy was done, and in 86 per cent of those in

10. Ivarsson, Robert: Eine Studie des Nierentuberkulosematerials aus der Lunder chirurgischen Klinik der Jahre 1901 bis einschliesslich 1923, Acta chir. Scandinav. (supp. 18) **68**:1, 1931.

which it was not done. Tuberculosis of the genitalia does not appear to be significant in the prognosis, but pulmonary tuberculosis constitutes a complication. Fifty per cent of the women with pulmonary tuberculosis died, whereas only 8 per cent of the women not so affected died. Corresponding figures for the men are 60 per cent and 26.8 per cent. Pulmonary tuberculosis is twice as prevalent among males as among females.

Initial hematuria occurred in 6.4 per cent of the cases, and in 3 of these, it was from one to two years before the next symptom appeared. Microscopic pyuria was present in all cases. In the cases in which the bacillus of tuberculosis was not found in the urine, advanced renal tuberculosis was usually present. Eight and six-tenths per cent of the 105 male patients had urethral stricture. In spite of repeated cystoscopic examinations and treatment by bougies, there was no definite case of miliary tuberculosis.

Of the 156 cases in which one kidney was removed, there was injury to the pleura in 1 case during the operation and to the peritoneum in 4 cases; in all of these cases the lesion was sutured, and complications did not occur subsequently. In another case a lesion occurred in the peritoneum, which was not detected, and the patient died of septic peritonitis. In 52 per cent of the cases the nephrectomy wounds healed within two months. If perinephritic adhesions were marked, only 32 per cent healed within the same time. Of the 155 patients traced, 101 (65.2 per cent) are alive, and 55.5 per cent are considered fully recovered. Fifty-four patients (34.8 per cent) have died.

The cause of death within the first six months was generally miliary tuberculosis or tuberculous meningitis, whereas the cause later seemed to be secondary infection.

In most of the 35 cases in which nephrectomy was not performed, there was generalized miliary tuberculosis, and such radical procedures were not indicated. Twenty-eight of these patients died during the first year. Three were clinically cured of the renal tuberculosis, and 1 patient continued to work for nineteen years.

[Compilers' Note.—Ivarsson's statistics compare favorably with with those of other large groups, particularly in relation to associated extrarenal tuberculosis. Condamin[11] studied a series of 172 cases of renal tuberculosis in which there was no extrarenal lesion. Nephrectomy resulted in cure in 69 per cent of cases; the operative mortality was 2.9 per cent, and the late mortality was 27.5 per cent. In contrast to this, in a group of 53 cases of both renal and extrarenal tuberculosis,

11. Condamin: Des tares apportées aux résultats de la nephrectomie pour tuberculose unilatérale par des localisations tuberculeuses extra-rénales, J. d'urol. **21**:31, 1926.

nephrectomy resulted in cure in only 47 per cent. Nine per cent of patients with coexisting pulmonary tuberculosis died following operation, and only 29 per cent recovered completely. Lesions of bone have the least effect on the ultimate results: In 62 per cent of 18 cases complicated by lesions of bone, complete recovery occurred. In 59 per cent of 12 cases of genital lesions, recovery took place. Persson [12] reported 295 cases from the Seraphimer Hospital, Stockholm. Symptoms of other tuberculous lesions occurred in about half the cases as follows: pulmonary tuberculosis, 66 cases (22.4 per cent); tuberculosis of genitalia (male), 46 cases (15.6 per cent); tuberculosis of bones and joints, 21 cases (7.1 per cent); pleuritis, 7 cases, and lymphadenitis, 10 cases. There were 84 cases in Persson's series in which operation was not done. Death occurred in 71 cases (84.5 per cent). In Wildbolz' [13] large series of cases, more than half of the patients who had been traced from ten to twenty years following nephrectomy died of tuberculosis of the remaining kidney or of pulmonary tuberculosis. Rovsing and Frode [14] reported 632 cases of renal tuberculosis; 62 per cent of the patients were well following nephrectomy. Death usually occurred within the first year after nephrectomy and, as in Wildbolz' cases, was generally due to tuberculosis of the remaining kidney or other organs.]

Papin and Bordas [15] reviewed 400 cases of hematuria which followed nephrectomy for tuberculosis of the kidney. The hematuria was classified according to the time of appearance: immediately following operation, during the course of the postoperative period and weeks, months or even years afterward. The hemorrhage may come from the ureteral stump, from the opposite kidney or from the bladder. It is generally slight and attracts little attention. In the early days following operation it is reasonable to believe that it was the remaining kidney that was bleeding. This cannot be demonstrated positively, as cystoscopy at this time should not be done unless it is absolutely necessary. The third type of hemorrhage occurs most frequently and is invariably from the bladder. In many cases the lesions have become worse after nephrectomy, sometimes becoming so serious that it has been necessary to exclude the bladder by an iliac ureterostomy. Occasionally hemorrhage from the bladder appears after conditions have quieted and the symptoms have disappeared or improved. This does not usually indicate that the second

12. Persson, Mauritz: Renal Tuberculosis: A Clinical Survey of 295 Cases, 90 of Which Were Not Operated On, Ann. Surg. **82**:526 (Oct.) 1925.

13. Wildbolz, Hans: Renal Tuberculosis, J. Urol. **21**:145, 1929.

14. Rovsing, Thorkild, and Frode, Rydgaard: Klinische Untersuchungen über die Tuberkulose der Harnwege, Bibliot. f. læger **117**:225, 1925; abstr., Ztschr. f. urol. Chir. **19**:415, 1926.

15. Papin, Edmond, and Bordas, Paul: Des hématuries chez les sujets nephrectomisés pour tuberculose rénale, Arch. d. mal. d. reins **6**:413, 1932.

kidney has become affected; iliac ureterostomy in grave cases has generally demonstrated the integrity of the remaining kidney.

Pascual[16] reported a case of tuberculous kidney in a man aged 37 years. There were no clinical symptoms, but roentgenograms revealed a complete shadow of the caseous and calcified organ as well as of the entire ureter from the kidney to the bladder. On cystoscopic examination the mouth of the left ureteral orifice was obliterated; the right side was normal. The bladder had normal capacity, and there was no ulceration or other signs of tuberculosis present. The kidney and ureter were removed, and a good result was obtained. The specimen proved to be a caseous tuberculous kidney with complete distortion and calcification of the organ and its thick blind ureter. The impression of petrified deposits occupying and obliterating both the kidney and the entire lumen of the pelvic ureter was obtained from the roentgenogram.

Pascual stated that this case indicates the need for complete urologic examination when dealing with a suppurating kidney, even though the premonitory symptoms have subsided and the silent kidney has undergone almost complete obliteration.

[COMPILERS' NOTE.—Renal occlusion occurs in about 10 per cent of the cases of chronic renal tuberculosis. Braasch stated that it can be recognized in about 90 per cent of cases. Symptoms such as pain, frequency and abdominal tumor may extend over a period of many years. The occluded kidney may be a focus of infection, especially if of recent occurrence. In several cases in which symptoms had been present for many years and the kidney occluded for from five to ten years, the bacillus of tuberculosis was found in the renal mass. If symptoms are present, nephrectomy is indicated; usually there is little risk in operating and good results are obtained, as satisfactory resistance to the infection has developed.]

Dossot[17] stated that tuberculosis of the kidney and of the renal excretory ducts may be easily confused. The latter is seldom present without participation of the renal parenchyma, but since the initial localization of the Koch bacilli is usually the point where the calices are inserted around the papillae, the lesions generally extend into the renal pelvis, ureter and bladder at the same time. Primary tuberculosis of the pyelo-ureteral tract is rare; approximately 12 cases only have been reported in the literature. In pyelo-ureteral tuberculosis the only constant lesion is ulceration of the lateral part of one or more papillae. The earliest lesions are in the noncaseous tuberculous follicles

16. Pascual, Salvador: Caseous Kidney, An. Hosp. de San José y Santa Adela (Cruz Roja) Madrid **2**:135, 1930-1931.

17. Dossot, R.: Tuberculose pyélo-urétérale, Arch. urol. de clin. de Necker **7**:135 (Dec.) 1931.

under the epithelium in the lateral portion of the papilla. As these lesions progress, they rapidly produce changes in the contractility of the pelvis and ureter, followed by modifications in the ability to evacuate the contents of the pelvis. After removal of a tuberculous kidney, tuberculosis of the ureter tends to regress and disappear, with the ureter contracting into a fibrous cord. There are cases in which the ureteral stump may give rise to further disturbances, such as persistence of cystitis and pyuria, purulent lumbar fistulas, urinary fistulas and formation of ureteral abscesses. To avoid these complications, two methods have been used: extirpation of the ureter at the time of nephrectomy; and simple nephrectomy followed by suitable treatment of the ureteral stump. Nephro-ureterectomy entails so much risk in cases in which the ureters are bound by inflammatory adhesions that it is not desirable; even when the patient recovers, postoperative fistulas are common. Systematic ureterectomy has been generally abandoned in favor of such measures as fixation of the stump to the abdominal wall, suture of the upper orifice of the ureter, or ligation and cauterization of the stump. All of these procedures are of doubtful value. Dossot prefers the technic of Legueu: section by thermocautery, between two clamps, of the ureter in the lower part of the lumbar wound; ligation of the ureter with catgut, and drainage if the perinephritis is intense, if pus has contaminated the region or if the surface of the kidney presents granulations. In the absence of such conditions, the wound is closed completely after the cavity has been filled with isotonic dextrose solution.

[COMPILERS' NOTE.—It is true that primary ureteral tuberculosis is seldom seen, because the original lesion is established in the kidney and the ureter becomes infected by the excretory bacilluria. The tuberculous ureter is the result of tuberculosis elsewhere in the upper part of the urinary tract, and when severe infection of the pelvis and ureter has been found, in a certain number of cases the conservative and safe procedure is to perform ureteronephrectomy in order to obviate lumbar fistula, pyuria, tuberculous cystitis and other common sequelae. Kelly, Beer, Gutierrez, Papin, Judd and others heartily recommend this technic and have reported good clinical results without complications or fatalities. The technic of the operation of ureteronephrectomy in two stages is simple and may be carried out without difficulty; the results achieved justify its recommendation. Gutierrez [18] has recently described this operation.]

Katz [19] stated that tuberculosis is widespread not only among domestic fowls but among other birds, in various percentages. It usually

18. Gutierrez, Robert: Indications and Technic of Combined Ureteronephrectomy, Ann. Surg. **93**:511 (Feb.) 1931.

19. Katz, Traïan: Tuberculose urogénitale chez l'homme produite par le bacille de la tuberculose aviaire, J. d'urol. **31**:18 (Jan.) 1931.

affects the spleen, liver and intestinal tract. The kidneys are frequently involved, and in such cases localized or disseminated nodules are present. The bacillus differs from the human bacillus bacteriologically, morphologically, culturally and biologically. It grows more rapidly (in from ten to fourteen days) and at temperatures between 26 and 46 C.; the cultures are small, moist, abundant, mucofatty and slightly detachable, with a vitality far greater than that of the analog from human beings. The first case in man was published by Lipschutz in 1914, and 5 others have been reported since then. Katz has observed 2 cases, and concluded that the bacillus produces in man a septicopyemic disease known as morbus Löwenstein. It begins with fever (from 38 to 39 C. [100.4 to 102.2 F.]) which is not influenced by antipyretics. The general condition is not especially affected by this fever. Night sweats suggesting pulmonary tuberculosis and enlargement of the spleen are observed. After this phase, which may last months or years, localization is reached, with the site of predilection in the kidneys, bone marrow and the skin. Small yellow nodules from 1 mm. to 1.5 cm. in size are found in the kidneys; in rare cases there is cavity formation with caseation. Diffuse cystitis is characteristic but without specific lesions. The presence of large numbers of acid-fast bacilli with the polymorphonuclear leukocytes is always suggestive of tuberculosis of avian origin. Their portal of entry is probably through the mouth, with the ingestion of food, particularly eggs containing the bacilli. Löwenstein infected hens' eggs with avian bacilli, boiled the eggs and later recovered living bacilli from the hard-boiled eggs. Histologically, the affected tissues do not exhibit tuberculosis but abscesses and disseminated necrobioses. If treated early, these patients are readily cured by injections of avian tuberculin. Spontaneous cure occurred in 1 case on record.

*Cysts.*—Covisa [20] emphasized the rarity with which hydatid cysts are localized in the genito-urinary organs. The highest estimate places them at 7.97 per cent of all such cysts. In 14,000 cases of genito-urinary disorders at the Provincial Hospital and in Covisa's private practice, there were only 9 cases of hydatid cyst, 4 of which were in the kidney and 5 retrovesicoprostatic. These four were open cysts in the renal pelvis, and were easily diagnosed. The symptoms were intermittent and sudden intense abdominal pains, followed by expulsion of foreign bodies resembling the seeds and skins of grapes. Eosinophilia was 5, 7 and 8 per cent in cases in which it was investigated.

Hydatid cysts may be opened or closed. The latter are difficult to diagnose, as they give few symptoms to distinguish them from other abdominal tumors. If small they are not noticed for some time and do

20. Covisa, I. S.: Hidatidosis genitourinaria, Rev. españ. de cir. y urol. **12**:552 (Dec.) 1930.

not cause symptoms; even when they are large the characteristic hydatid tremor cannot always be recognized. The diagnosis is based on investigation of eosinophilia and fixation of complement, which is frequently positive. The closed cysts may become infected through the circulation of the blood and suppurate, complicating the symptoms by deep infection with intermittent fever and sudden profuse sweating, suggestive of closed pyonephrosis. When the cyst ruptures into the renal pelvis, the daughter cysts present the clinical picture of nephritic colic and are expelled in the urine. The tumor becomes reduced in size, but the cysts generally fall a prey to infection, and pyonephrosis develops, which ends by destroying the entire renal parenchyma. The formation of firm perinephritic adhesions then renders operative procedure difficult.

Treatment is necessarily surgical. The methods used have ranged from simple puncture to marsupialization of the cystic pouch, after sterilization of its contents, the evacuation and capitionnage of the cyst and its extirpation with or without simultaneous nephrectomy. The procedure chosen must depend on the intrinsic conditions of the cyst, such as its size, adhesions and relations to the kidney and its pelvis. A cyst can rarely be removed in one piece because of adhesions. Small cysts may sometimes be removed by partial nephrectomy. Large cysts usually require marsupialization, but the tendency of purulent or urinary fistulas to form must be borne in mind. Recurrence is common. Nephrectomy should be done by the lumbar route in order to avoid infection. It is the method of choice when partial nephrectomy is impossible and marsupialization is not necessary, for it has the advantage of prompt and radical cure without recurrence, provided the contents have not ruptured into the perirenal tissues.

According to the literature, retrovesical hydatid cysts are more rare than renal cysts. They may cause grave urinary disturbances, and are generally recognizable by the fact that the hypogastric tumefaction persists after catheterization of the bladder. If there is suppuration, diagnosis is more difficult, small cysts being easily confounded with abscesses of the prostate gland and seminal vesicles. These cysts may be due to a generalized peritoneal hydatidosis, or they may be the sole peritoneal localization. The prognosis is more favorable in the latter instance. The treatment of choice is marsupialization, preferably hypogastric. The retroperitoneal evolution of the cyst may make the perineal route more convenient in some cases. Its complete extirpation in a mass is generally not feasible because of adhesions. Eight clinical cases are reported.

Munger [21] stated that the hemorrhagic type of cysts of the kidney are caused by hemorrhage into a cyst of varied origin, and that such

21. Munger, A. D.: Acute Hemorrhagic Cyst of Kidney, J. Urol. **27**:73 (Jan.) 1932.

lesions should be grouped according to the histogenesis. A case of a cyst of lymphogenic origin, with hemorrhage, is reported by Munger. These cysts are relatively rare and do not present a characteristic syndrome. Treatment is surgical; nephrectomy is preferred when resection is not possible.

*Carbuncle.*—Brady [22] stated that carbuncle of the kidney is caused by metastatic staphylococcal infection, which frequently is limited to the cortex; the pelvis of the kidney is not involved. The infection is usually secondary to furuncle, abscess or carbuncle of the skin or subcutaneous tissue. The typical carbuncle is composed of many small suppurating areas, and the whole lesion is separated from the remainder of the kidney by a definite ring of inflammatory tissue. Perinephritic abscess often develops from the carbuncle. It is the belief of some surgeons that all perinephritic abscesses arise in this manner, although the cortical lesions are not always detected. Microscopic examination of a carbuncle of the kidney shows lymphocytes, plasma cells and polymorphonuclear leukocytes. Staphylococci are usually scattered through the tissues.

A study of the literature revealed 88 reported cases of carbuncles of the kidney. The lesion occurred most frequently between the ages of 20 and 40 years. Fifty-four carbuncles occurred in men and 21 in women. In 13 cases the sex was not recorded. In 73 cases there was a definite history of a primary focus from which organisms could be carried to the kidney, and in 3 others there was a history of trauma to the side on which the carbuncle developed. The usual time between the onset of the primary focus and the carbuncle of the kidney was one month, although there were a few cases in which seven months elapsed between the onset of the primary focus and the development of the carbuncle of the kidney.

The onset of symptoms of this disease is usually acute; occasionally they appear gradually. Sometimes the temperature is elevated for a month before any renal lesion is indicated. On palpation there is localized tenderness over the involved kidney, and later a mass can often be felt. Cystoscopy in 23 cases did not disclose any abnormality in the appearance of the bladder and ureteral orifices. In almost every instance in which a differential phenolsulphonphthalein test was done there was delay in the appearance of the dye from the affected side, and diminution of the phenolsulphonphthalein excreted from the kidney containing the carbuncle as compared to the other kidney. In 43 cases it was noted that a perinephritic abscess was present. Positive cultures were obtained at operation directly from the carbuncle in 65 cases. The records do not

22. Brady, Leo: Carbuncle of Kidney (Metastatic Staphylococcus Abscess of Kidney Cortex), J. Urol. **27**:295 (March) 1932.

indicate whether cultures were taken in the remaining cases, but there is no mention on this subject of a negative culture being obtained from a renal carbuncle. In 45 cases Staphylococcus aureus was present; in 3 cases, Staphylococcus albus; in 14 cases the type of staphylococcus was not reported.

In 39 cases nephrectomy was performed at the first operation. There were 3 deaths (7.7 per cent). In the 45 cases in which different conservative procedures were carried out, there were 5 deaths (11 per cent). Four of the 5 patients who died were treated by incision and drainage of the carbuncle, and the fifth was treated by enucleation of the carbuncle and later by nephrectomy. Two of the 5 patients on whom nephrectomy was performed after a primary conservative operation died. Five patients treated by excision of the carbuncle and 2 whose kidney was incised and soaked in a flavine dye recovered. In Brady's personal case the renal capsule was divided through its entire length and drained down to the carbuncle; the result was satisfactory.

Brady's conclusion, after reviewing these 88 cases of renal carbuncle, is that no definite rules can be drawn for the precise operation indicated. He favors some type of conservative procedure; in a large number of cases the kidney can be saved by incision and drainage of the infected area.

MacMyn [23] described carbuncle of the kidney as staphylococcal suppurative nephritis, the result of hematogenous metastatic infection of the parenchyma of the kidney following a suppurative lesion of the skin such as a boil, whitlow or carbuncle. It produces a localized necrotic zone in the renal substance with multiple suppurative foci, and later circumscribed abscesses form with enlargement of that part of the kidney involved in the infectious process.

The onset of the symptoms is gradual; headache, fever and malaise appear several weeks after the primary infection. Lumbar pain in the side involved, with tenderness and rigidity, appear later. Usually there are no urinary symptoms, and because the lesion does not communicate with the renal pelvis or calices the urine may be normal. Pyelograms may be negative, although if the condition is advanced there will be a compression defect or distortion of the calices. The significant diagnostic facts are the history of infection of the skin, the gradual onset of malaise, fever, pain and tenderness in the lumbar region and comparatively normal urine.

Nephrectomy is usually indicated. More conservative measures, such as drainage, enucleation or heminephrectomy, are not sufficient, and subsequent nephrectomy is almost always necessary. More careful explora-

23. MacMyn, D. J.: Carbuncle of the Kidney, Brit. J. Urol. **4**:11 (March) 1932.

tion during operations for perinephritic abscess will show a higher percentage of carbuncles of the kidney than have been previously reported.

*Rupture.*—Pedroso [24] reported on closed traumatism of the kidney, that is, injury in which there is no external wound of the integuments of the organ. The injury may be caused by direct or indirect contusions, the form depending on the force of the blow, the resistance offered and the point of support. In 1 of 2 cases, a boy, aged 10 years, apparently received abdominal injuries by a fall. Laparotomy done twice did not disclose trauma of any abdominal organ, but the second operation established the presence of a huge retroperitoneal tumefaction occupying the renal fossa on the left side, which had not been present at the time of the first operation. Three weeks after the injury, nephrectomy was performed and an infected hydronephrotic sac was found. The unusual feature of this case was the apparent rapidity with which traumatic hydronephrosis developed, and also the fact that the kidney was in a state of advanced atrophy only three weeks after the lesion had occurred.

As a rule, authors deny the possibility of primary traumatic hydronephrosis. Proof of the existence of the condition in this case is demonstrated by the fact that prior to the accident there were no symptoms; that at the first laparotomy there was no tumor; that the tumor doubled in size during the four days preceding nephrectomy, showing the rapidity of its growth, and that at nephrectomy, three weeks after the injury, the tumor contained the multiple cavities with condensation of parenchyma characteristic of hydronephrosis. Pedroso is of the belief that the mechanism of this hydronephrosis lay in the obstruction of the ureteral orifice by blood clots. Expectant treatment is justified only in benign cases. In every case of renal tumefaction, internal hemorrhage of forty-eight hours' duration or persisting slight hematuria, surgical intervention should be carried out.

Lazarus [25] stated that hydronephrotic kidneys are more prone to spontaneous and traumatic rupture than normal kidneys. Henline found only 24 cases of spontaneously ruptured kidneys reported in the literature; 19 of these patients were operated on, and 7 died. The 5 patients not operated on died. Spontaneous rupture of kidneys may be due to mild forms of trauma, which may be easily overlooked by patients. The rupture occurs rarely, as indicated by the few cases reported in the literature. Kidneys of children which rupture as a result of mild trauma are usually hydronephrotic.

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24. Pedroso, Gonzalo: Closed Traumatisms of the Kidney, An. d. cir. **3**:112 (March) 1931.

25. Lazarus, J. A.: Traumatic Rupture of Congenital Hydronephrotic Kidney. Ann. Surg. **95**:117 (Jan.) 1932.

Exploratory laparotomy is indicated in cases in which there is doubt regarding the presence of an intra-abdominal lesion associated with the renal injury. The kidneys should be exposed and explored through a second incision in the loin. Conservative surgical measures cannot be used in cases of rupture of congenitally hydronephrotic kidneys; nephrectomy is the procedure of choice.

*Nephritis.*—Simons [26] stated that surgical intervention is indicated in selected cases of acute and chronic nephritis in which one or more of the following symptoms are present: severe renal pain, massive renal hemorrhage, the oliguria-anuria-uremia complex and the preceding symptom associated with anasarca.

Complete urologic examination should be made in order to eliminate conditions such as hemorrhage with tuberculous kidney, calculous anuria, neoplasm of the kidney or its pelvis and other conditions which are not true manifestations of nephritis.

Most of the cases which are considered as surgical are classified in the groups as acute diffuse glomerulonephritis, chronic diffuse glomerulonephritis, the kidney of pregnancy and eclampsia, necrotic nephroses, lipoid nephroses, embolic purulent nephritis and focal and unilateral nephritis. Renal decapsulation, nephropexy, nephrotomy and nephrectomy are indicated in selected cases. Simons emphasized the point that the various forms of chronic nephritis without anuria are not suitable for decapsulation. In the early history of renal surgery Edebohls, Guiteras and others advocated this procedure in these cases and to a certain extent brought the operation of decapsulation into disrepute.

Randall, in considering nephritis, cited the recent work of Richards in regard to nephritis which accompanies poisoning with corrosive mercuric chloride. In Richards' experimental work it is pointed out that the primary effect is destruction of tubular epithelium. Tubules are filled with their own detritus, a process which continues for about ten days, during which time there are symptoms of anuria and increasing changes in the chemical composition of the blood. Usually with the administration of increased fluids these tubules gradually empty themselves, and the anuric state is terminated. It was observed that, although clinically the anuria was ended and urination was apparently normal, the chemical changes in the blood increased and reached a maximum only in about three or four days after the anuria had been broken. Richards' explanation of this is that when the tubules have been washed free of cellular detritus they are almost denuded of epithelium. Glomerular fluid coming down and passing through the tubules is separated from the vascular bed of the kidney by a thin membrane, and

26. Simons, Irving: The Surgical Treatment of Nephritis, J. Urol. **27**:399 (April) 1932.

a vicious cycle is created whereby the tubular fluid is immediately reabsorbed. In spite of the elimination of urine, there is no excretion of metabolic products, so for several days after the end of the anuria the chemical constituents of the blood may be expected to increase.

[COMPILERS' NOTE.—Renal decapsulation, nephrotomy and renal denervation are major procedures which have been tried with variable success for a number of years in treating nephritis. The operations have never become popular. Simons' extensive review of the subject is timely and in general agreement with the study by Rovsing published a few years ago. Undoubtedly the good results cited in selected cases of acute and chronic glomerulonephritis, in cases of pregnancy and eclamptic nephritides, in cases of massive hemorrhage and in general when the oliguria-anuria-uremia syndrome is present, with or without anasarca, will stimulate interest in chemical changes.

Randall's [27] presentation of Richardson's excellent hypothesis as to the cause of increasing retention of metabolite in the blood during the early phase of diuresis following poisoning by mercury offers a satisfactory explanation of this curious clinical paradox.]

*Regurgitation.*—Lewis [28] stated that urinary regurgitation has scarcely been mentioned among writers as a cause of sudden and severe renal colic without the source of it being discovered. Kelly and Burnham found records of more than 100 operations being performed, nephrectomy among them, for relief of this type of pain without discovering the etiology and without disappearance of the symptoms in many cases.

The pain is sudden and severe, at times requiring an opiate for relief; the attacks may recur at varying intervals. Examination by roentgen rays or ureteral catheterization fails to reveal any ureteral calculi.

Lewis has identified the etiologic factor in the majority of these cases as definite obstruction at the neck of the bladder. Removal of this obstruction has invariably given relief of the condition. The connection between obstruction at the vesical neck and renal colic was at first ascribed to reflex nervous influence. Since then it has been demonstrated that even a moderate amount of intravesical pressure is capable of overcoming the resistance of the ureteral valvular orifices and permitting the regurgitation of urine or fluid up into the ureters and renal pelves. The belief that this regurgitation causes the pain or colic has been confirmed by clinical results.

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27. Randall, Alexander: Surgical Treatment of Nephritis, J. Urol. **27**:468 (April) 1932.

28. Lewis, Bransford: Regurgitation Renal Colic, Urol. & Cutan. Rev. **36**:392 (June) 1932.

The diagnosis of this type of renal colic depends on conditions favoring back pressure and regurgitation through the ureteral orifices plus the inability to demonstrate the presence of stone in the ureter. If severe straining at urination with an over-filled bladder, accompanied by pain in either flank, indicates the presence of residual urine and there is no evidence of stone, a complete urologic examination should be made.

The prognosis of regurgitation colic depends on the removal and control of the obstructing factor.

[COMPILERS' NOTE.—Lewis deserves great credit for calling the attention of urologists to such an important and quite universally overlooked condition. In direct line with his consideration of this problem is the fact that renal colic from regurgitation in cases in which the ureteral meatus has been divided in the procedure of ureteral meatotomy causes distressing pain; on this account the operation is now avoided whenever possible. Doubtless back pressure from obstruction of the vesical neck has been overlooked as a cause of ureteral and renal pain, the basis being the mechanism which Lewis described.]

*(To be Continued)*